IN VITRO AND *IN SILICO* OF ALPHA GLUCOSIDASE INHIBITION AND ANTIFUNGAL ACTIVITY OF *COFFEA CANEPHORA* HUSK

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SUPLLEMENTARY MATERIAL

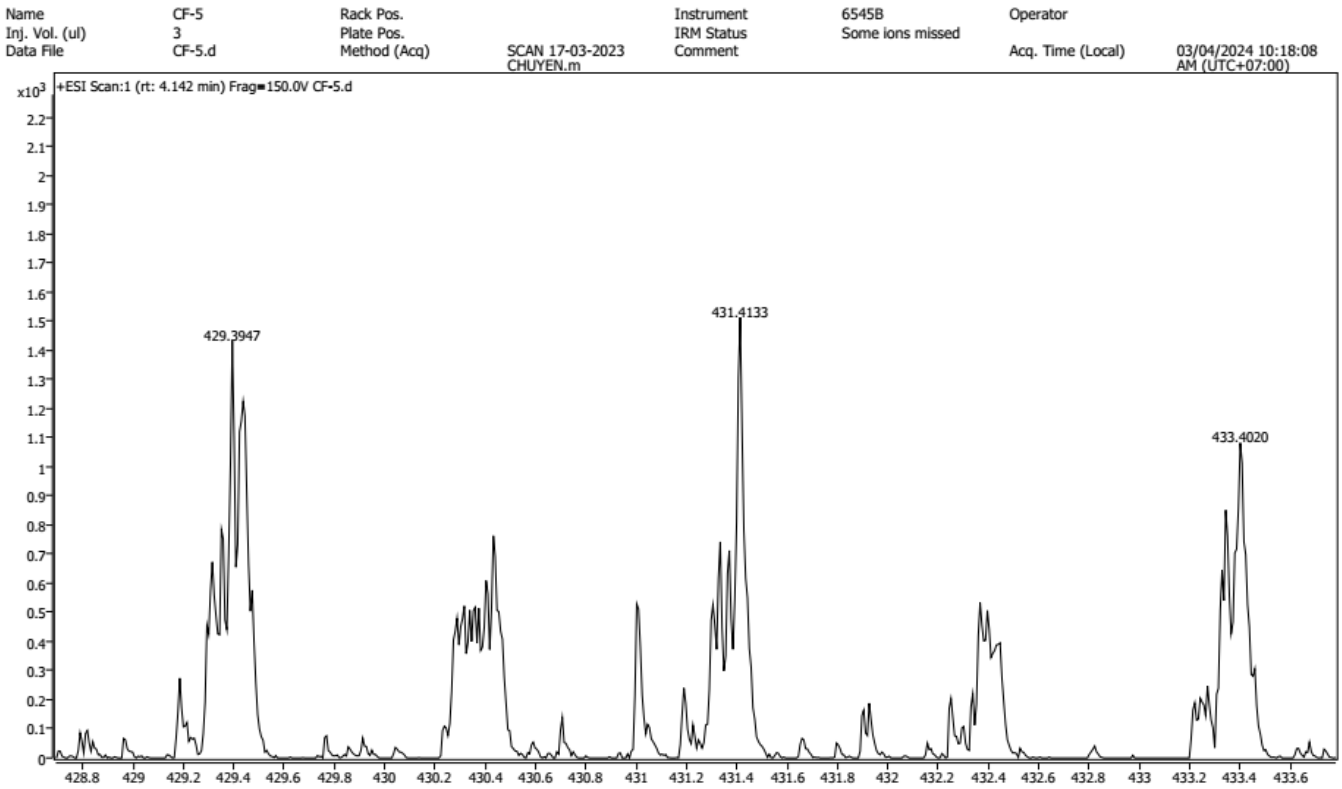


Figure 1S. The HR-ESIMS spectrum of **1**

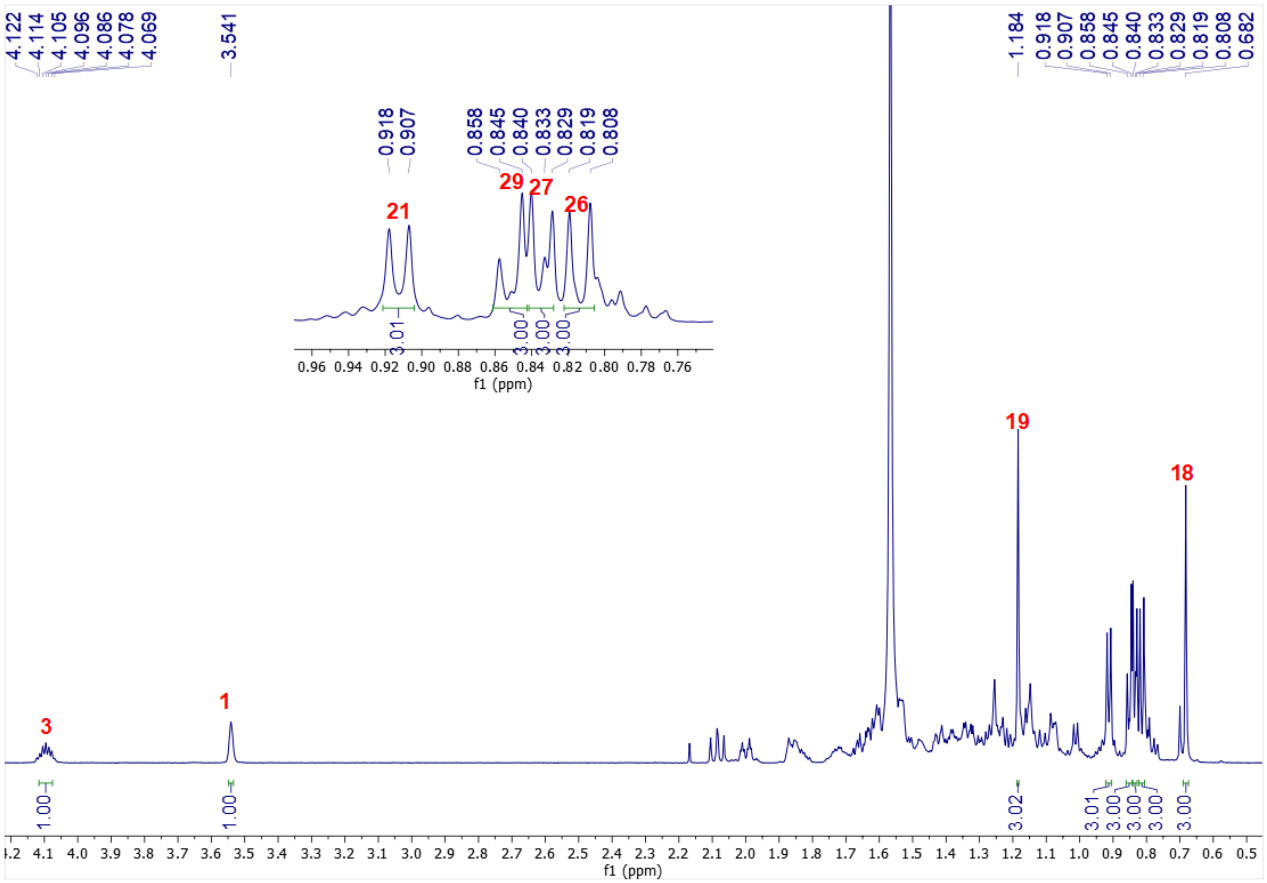


Figure 2S. The ^{1}H NMR spectrum of **1** in $CDCl_3$

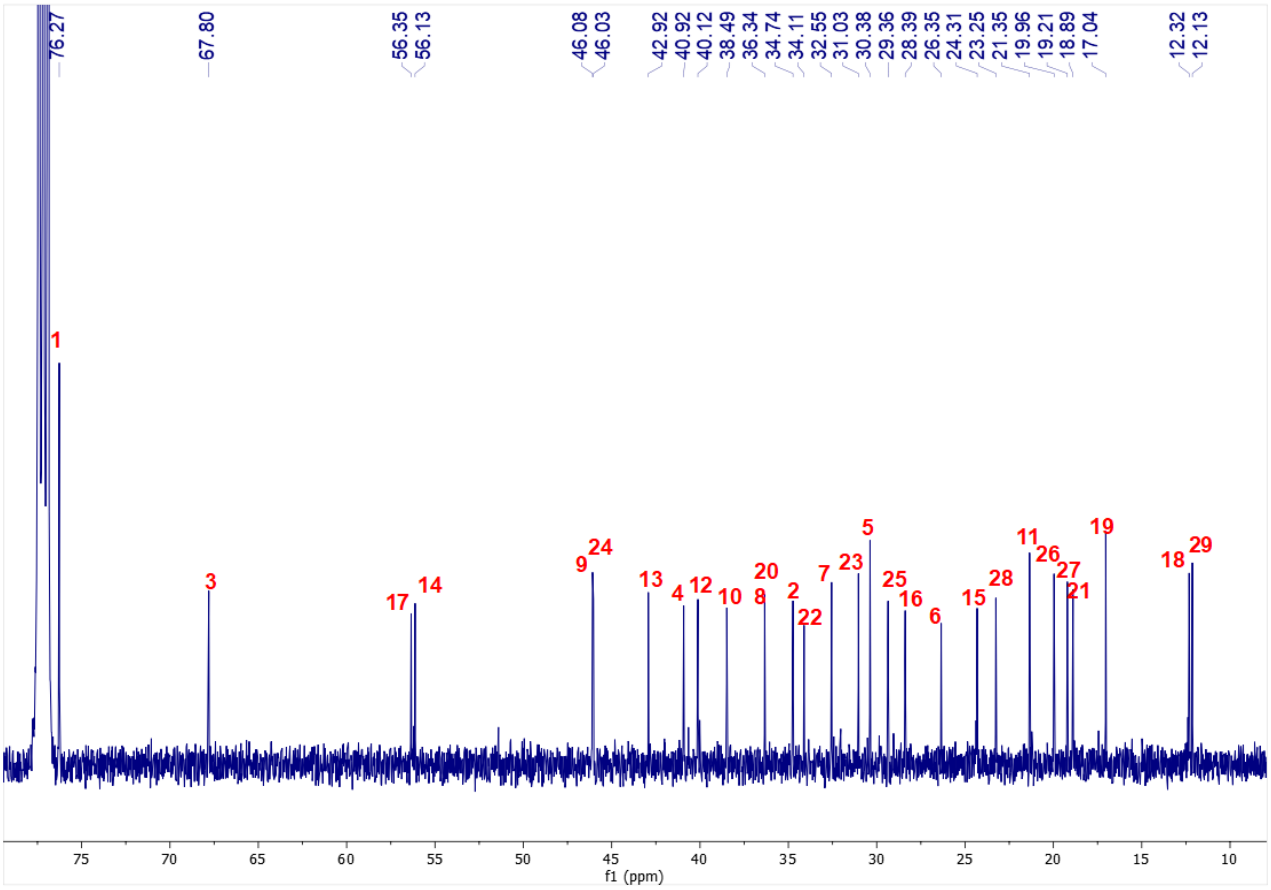


Figure 3S. The ^{13}C NMR spectrum of **1** in $CDCl_3$.

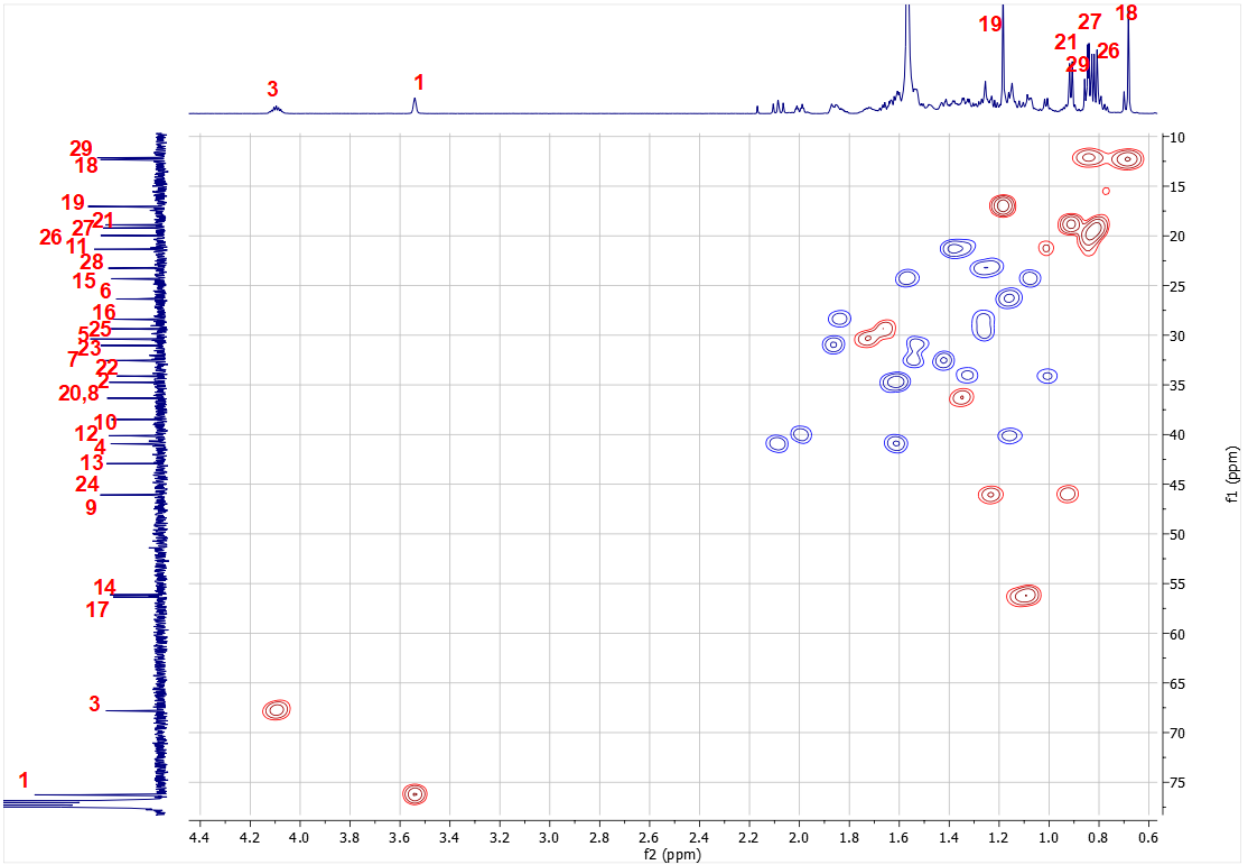


Figure 4S. The HSQC spectrum of **1** in $CDCl_3$

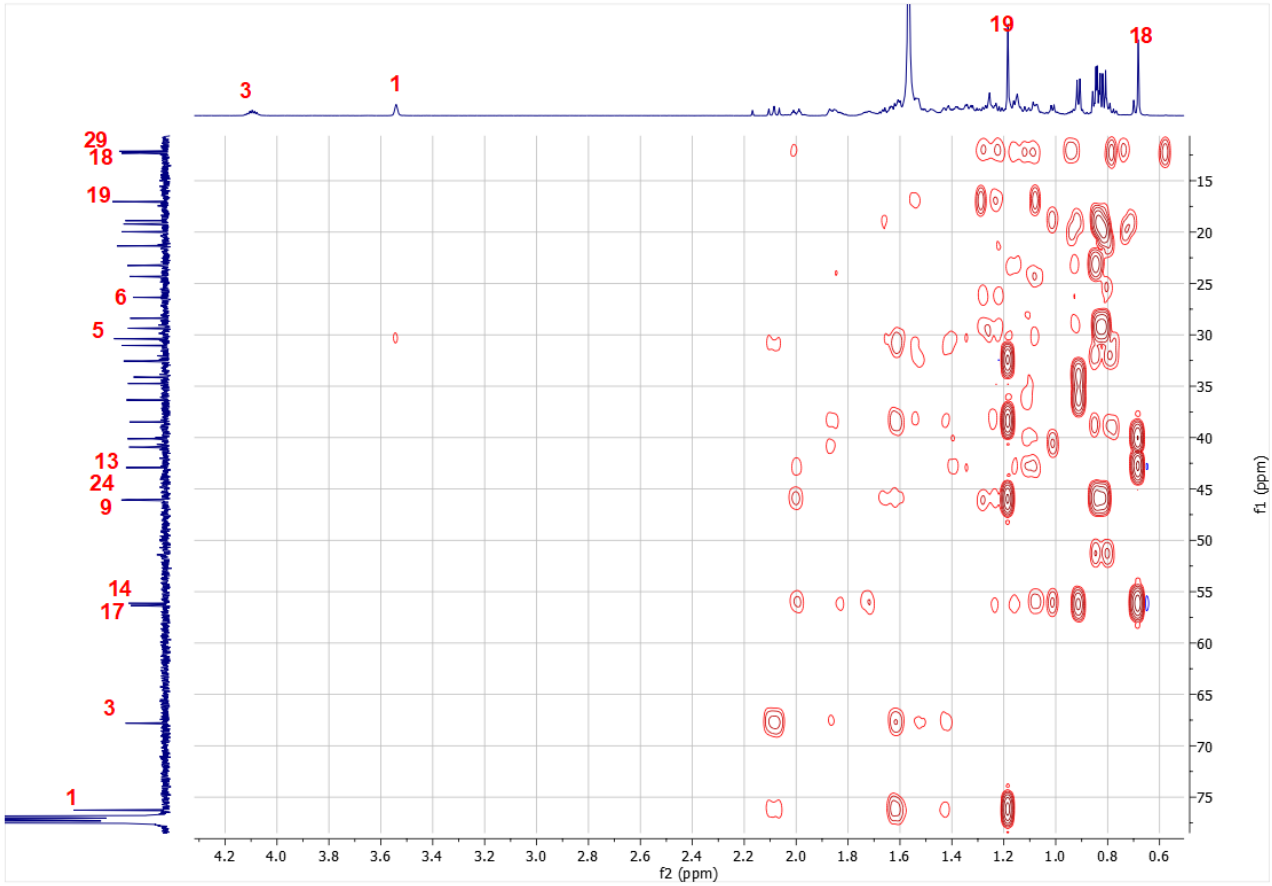
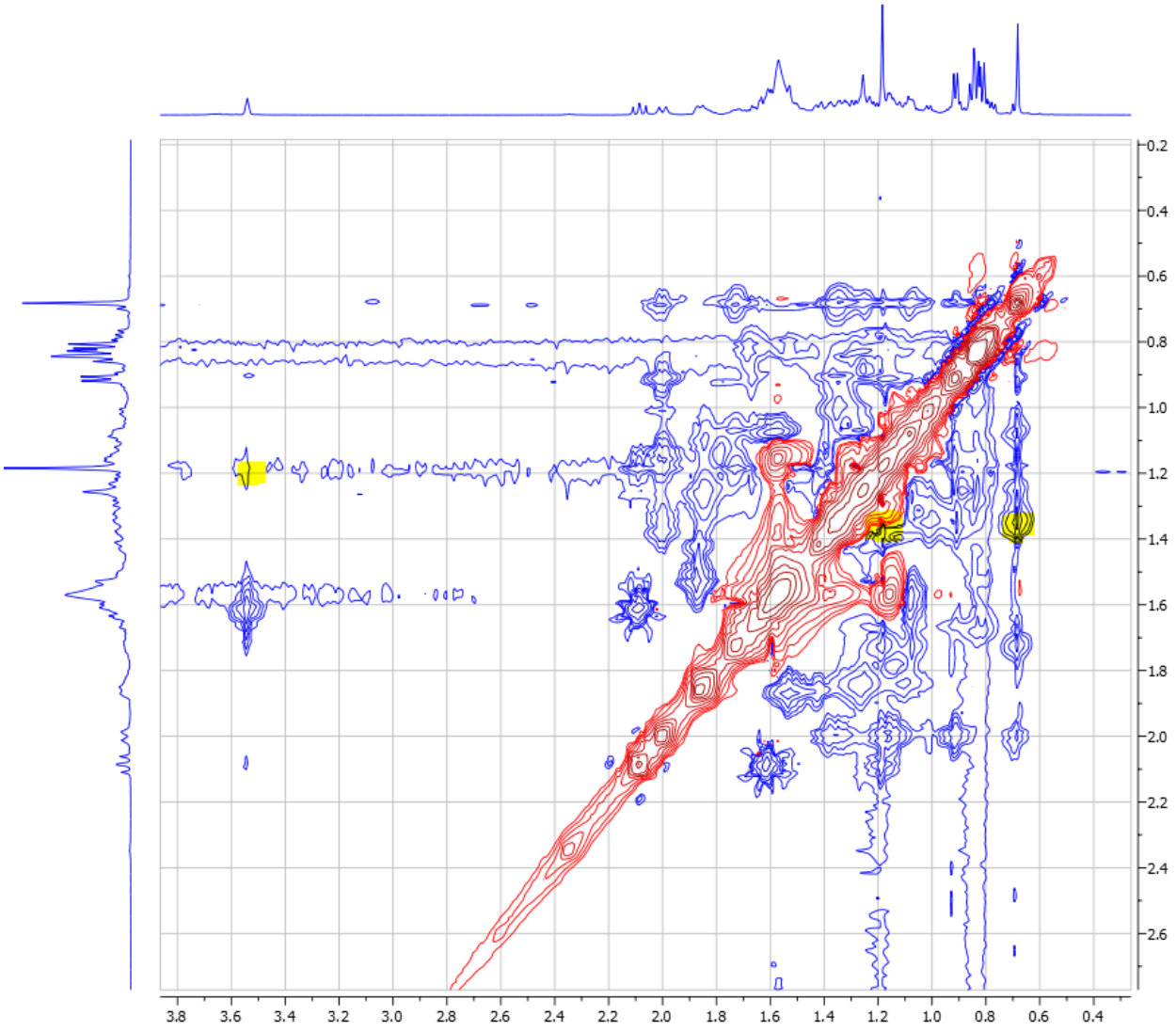


Figure 5S. The HMBC spectrum of **1** in $CDCl_3$


0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
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2.4
2.6
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4

Figure 6S. The NOESY spectrum of **1** in $CDCl_3$

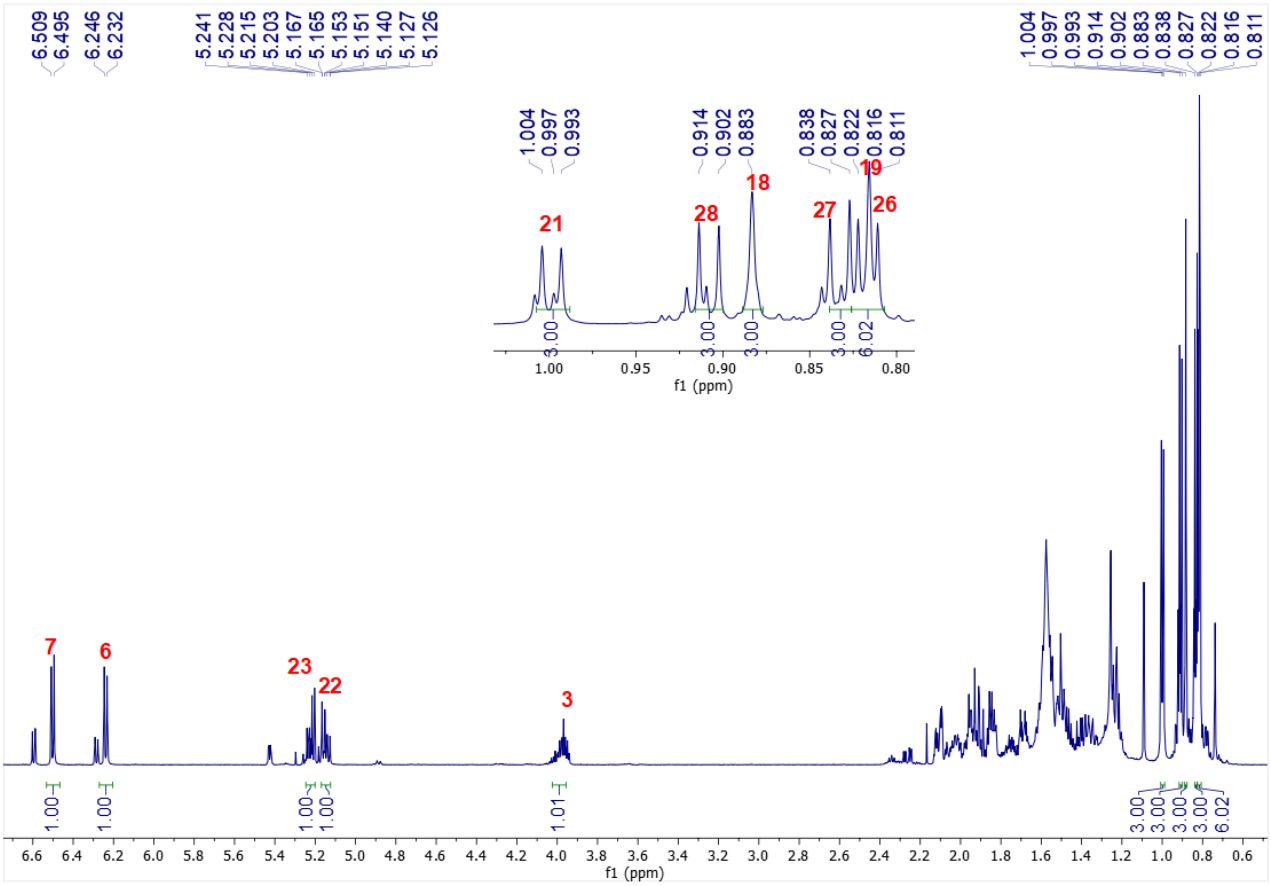

Figure 7S. The ^1H NMR spectrum of **2** in $CDCl_3$

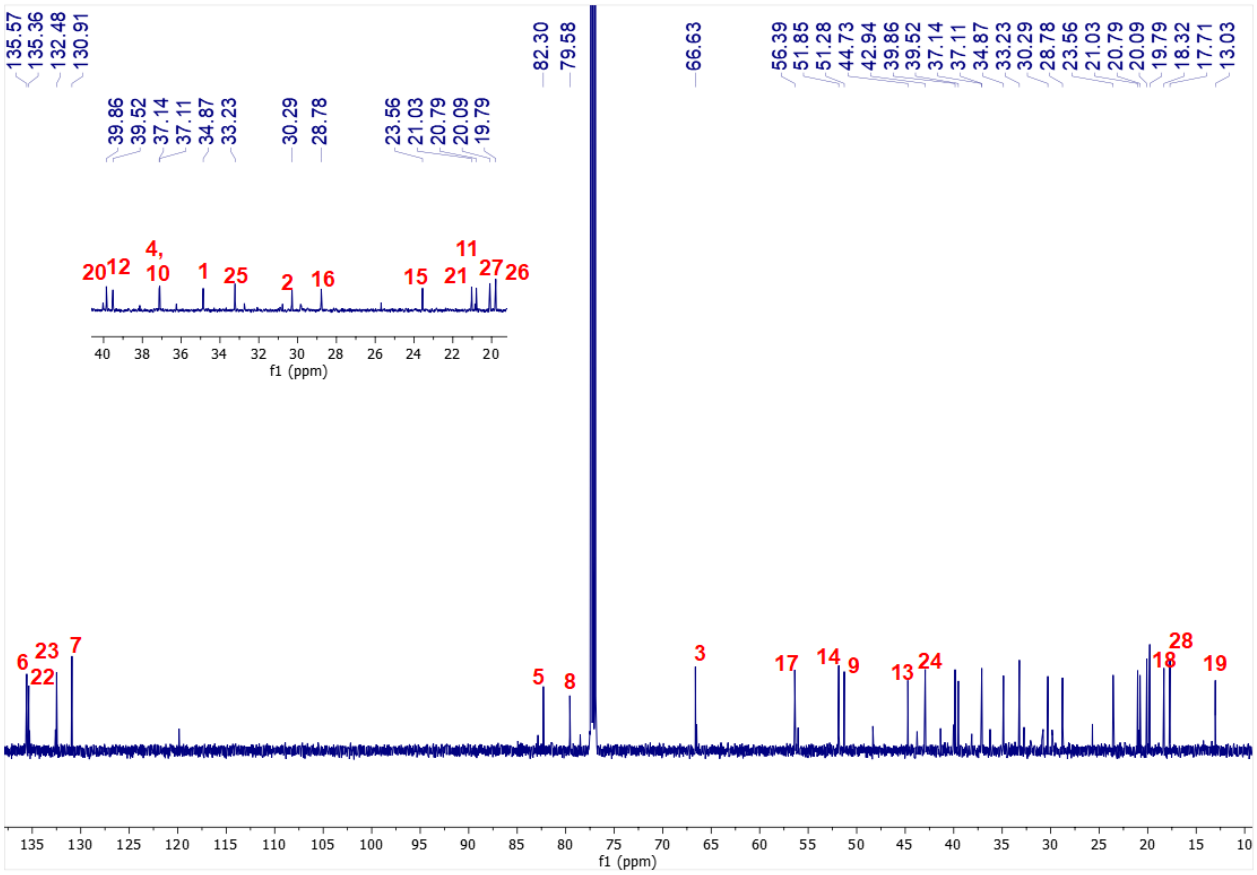

Figure 8S. The ^{13}C NMR spectrum of **2** in $CDCl_3$

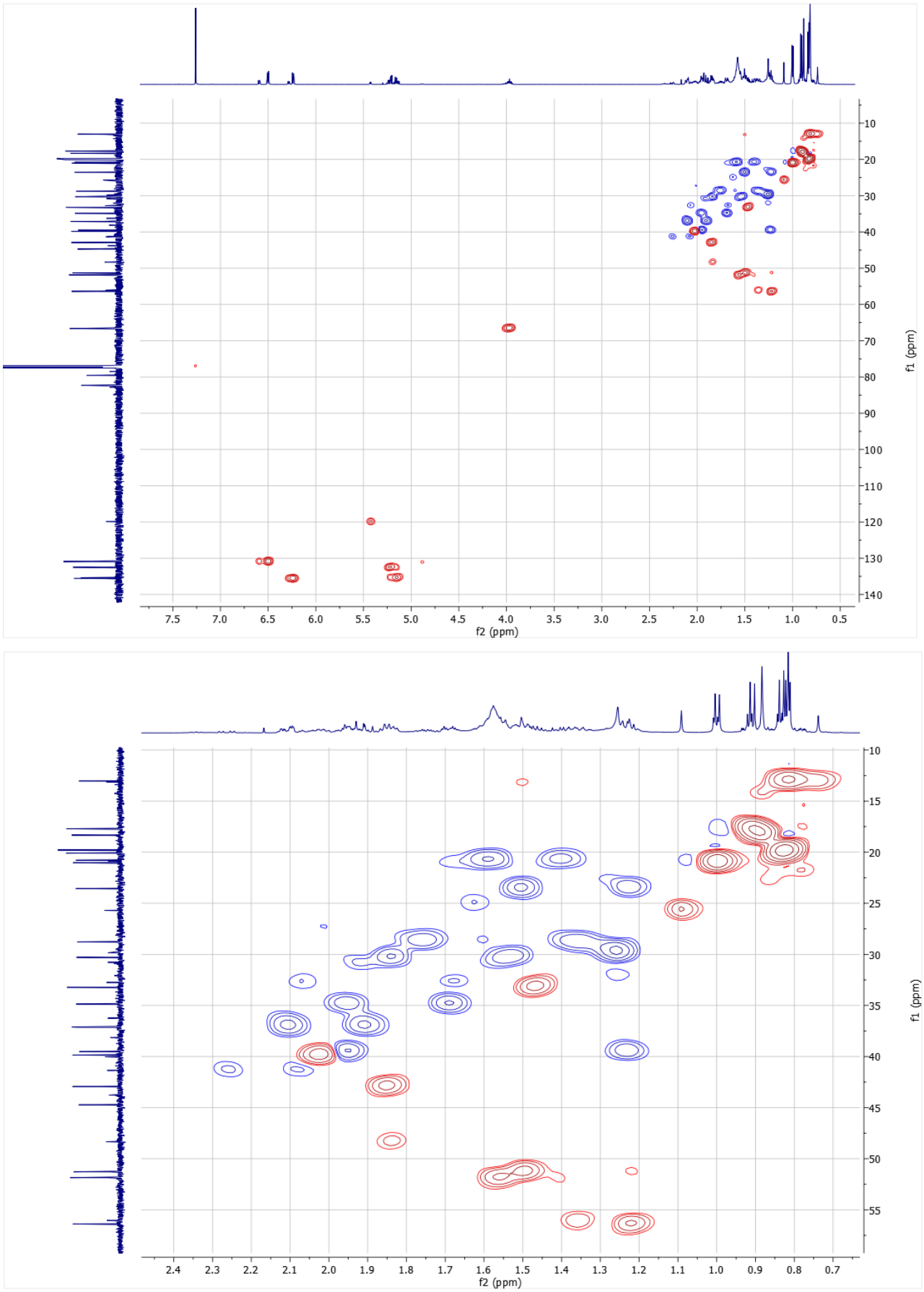

Figure 9S. The HSQC spectrum of **2** in $CDCl_3$

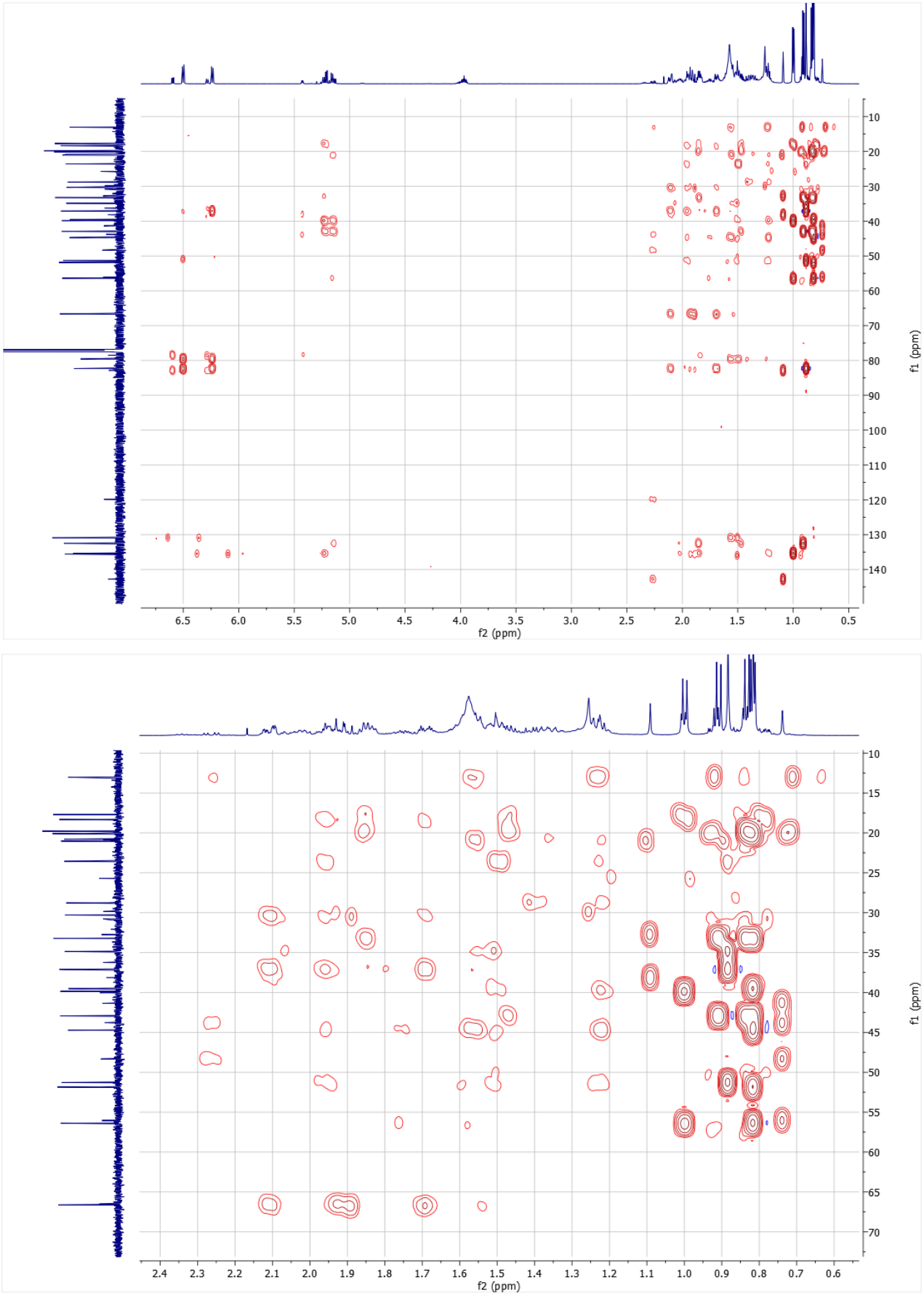

Figure 10S. The HMBC spectrum of **2** in $CDCl_3$

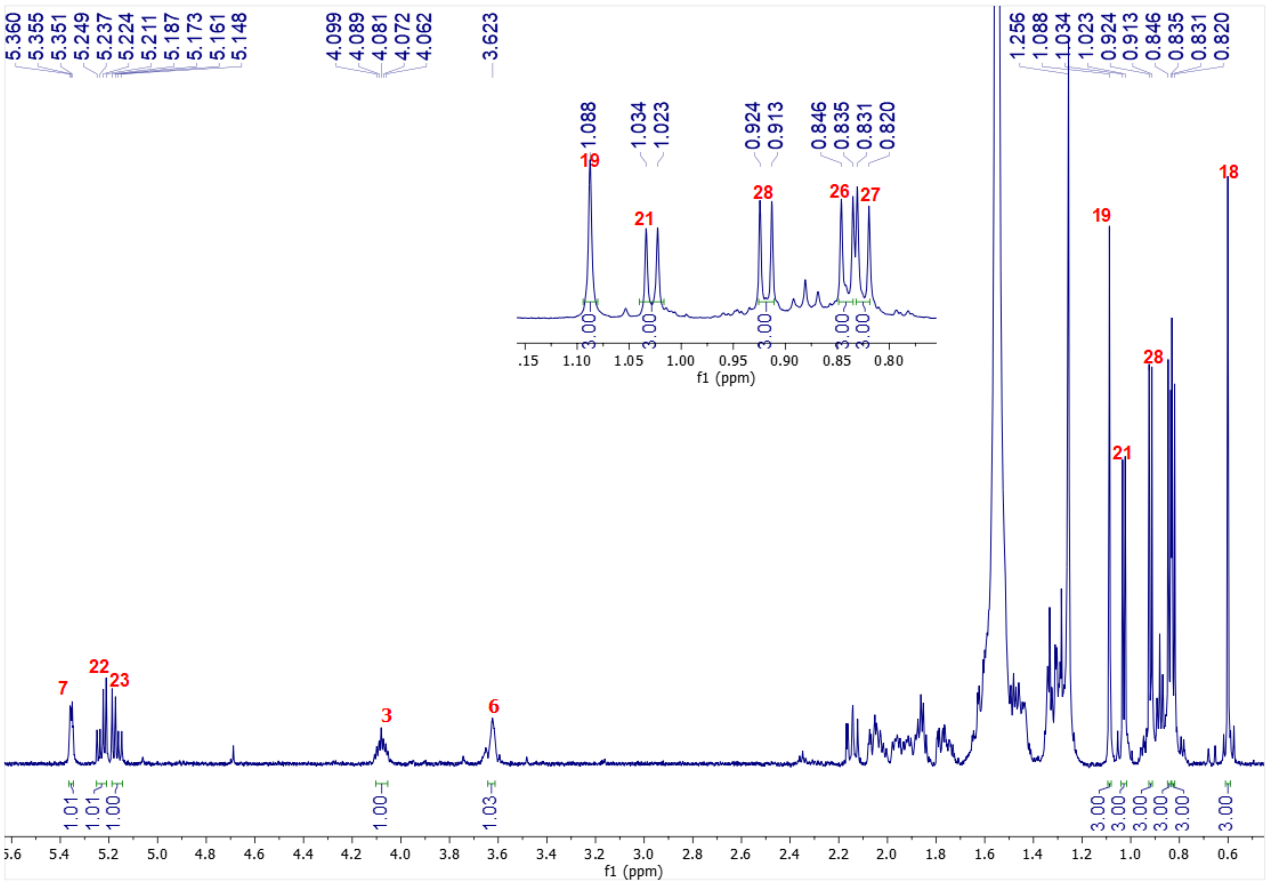

Figure 11S. The ^{1}H NMR spectrum of **3** in $CDCl_3$

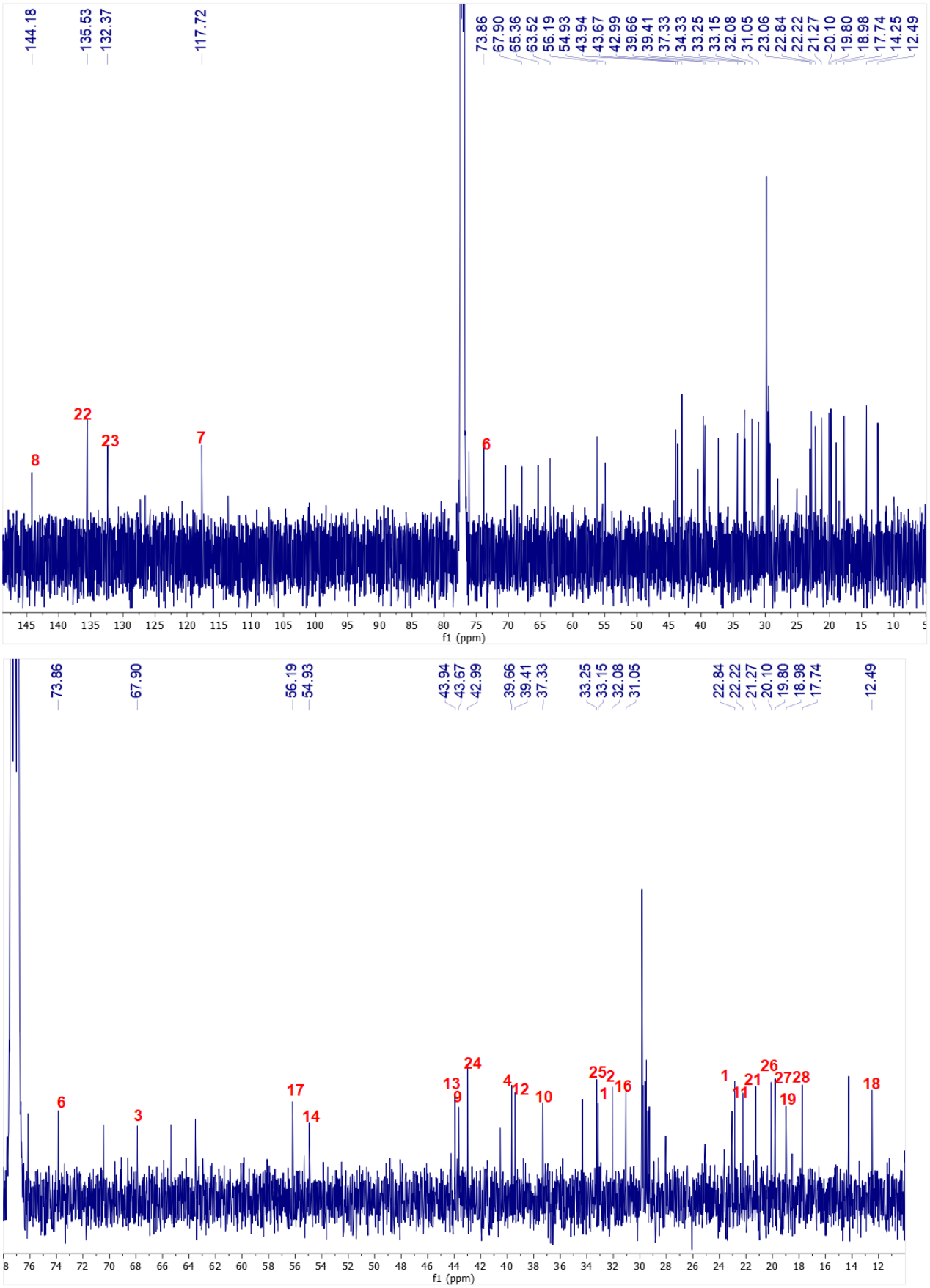

Figure 12S. The ^{13}C NMR spectrum of **3** in $CDCl_3$

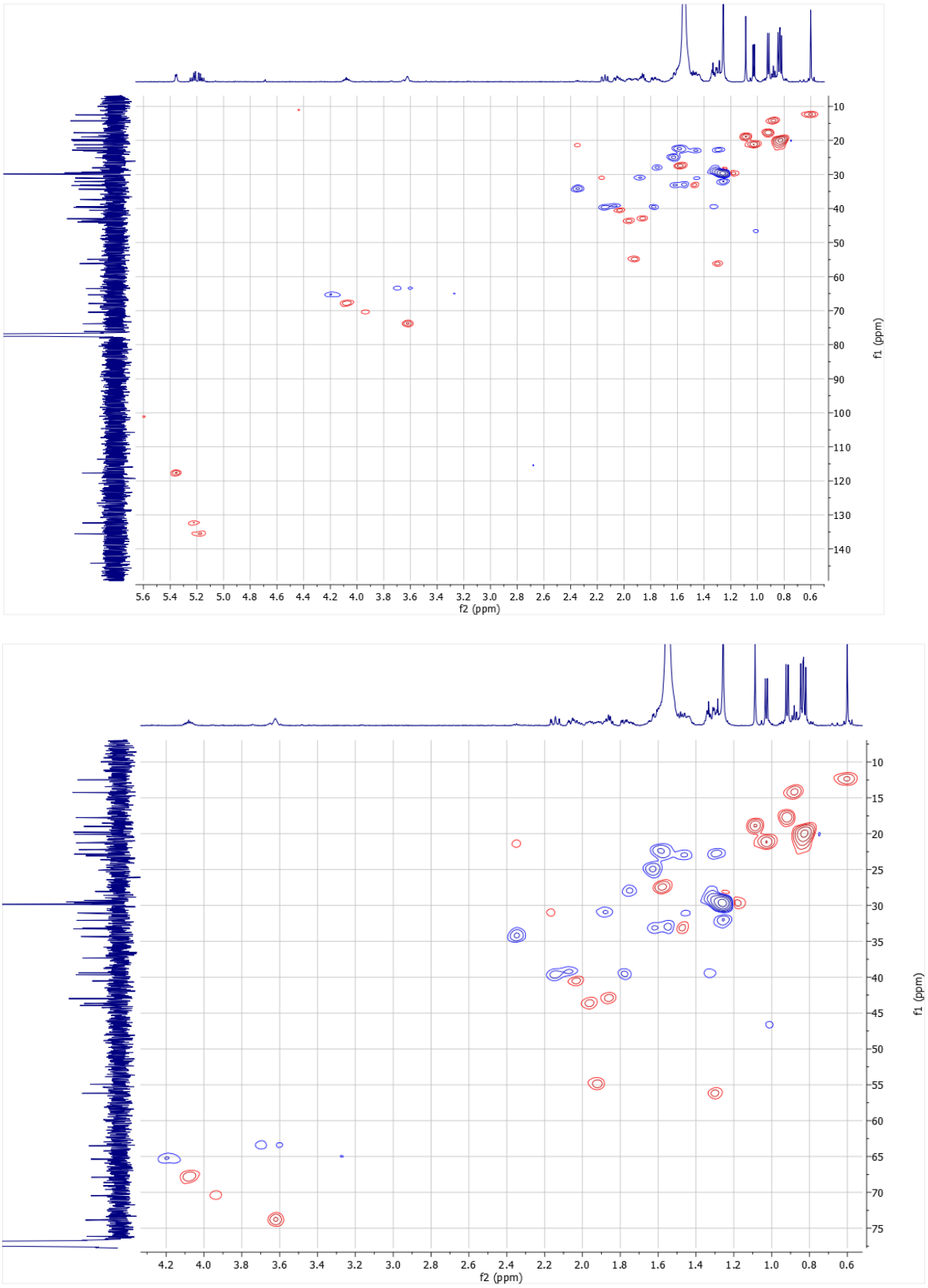

Figure 13S. The HSQC spectrum of **3** in $CDCl_3$

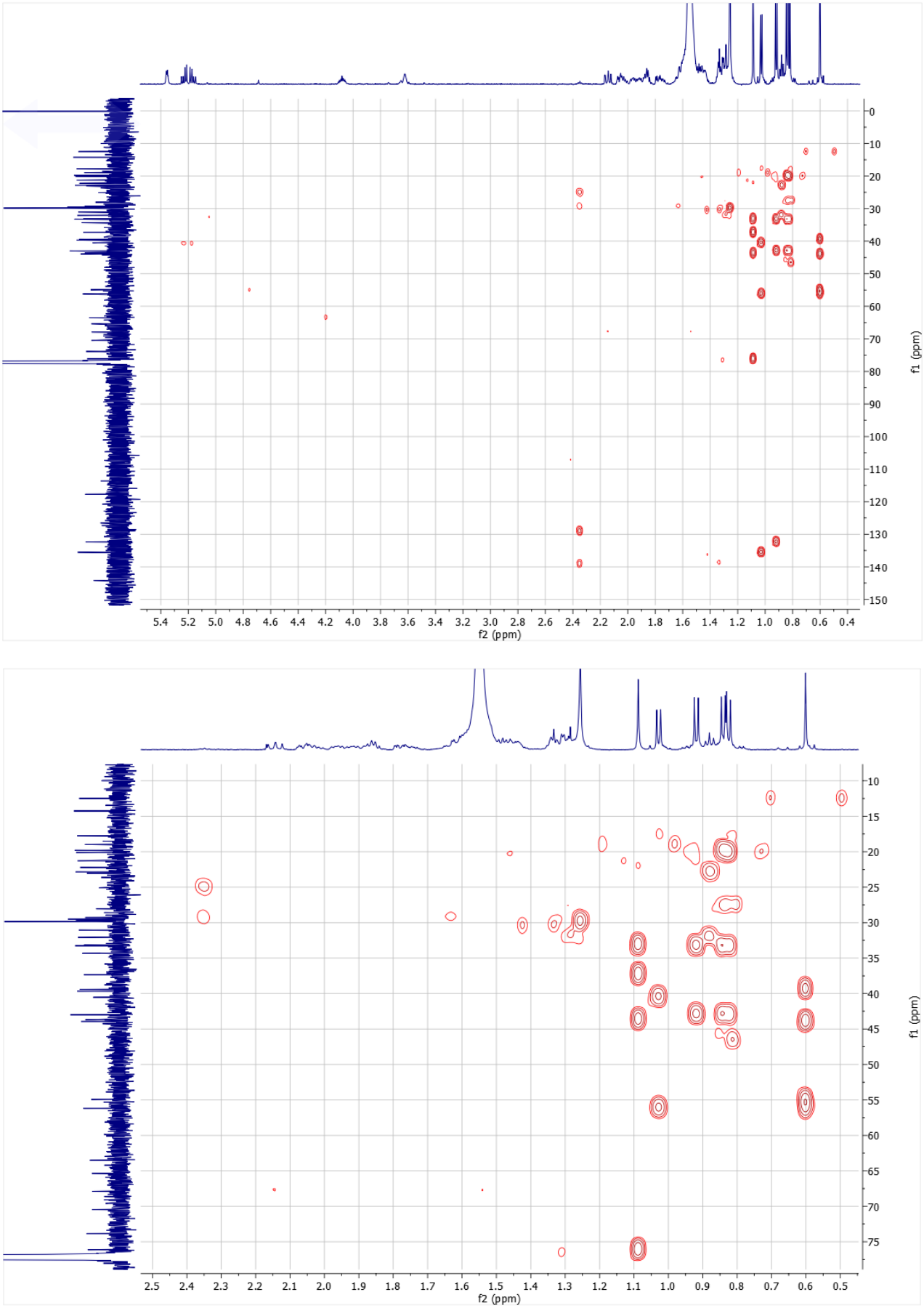

Figure 14S. The HMBC spectrum of **3** in $CDCl_3$

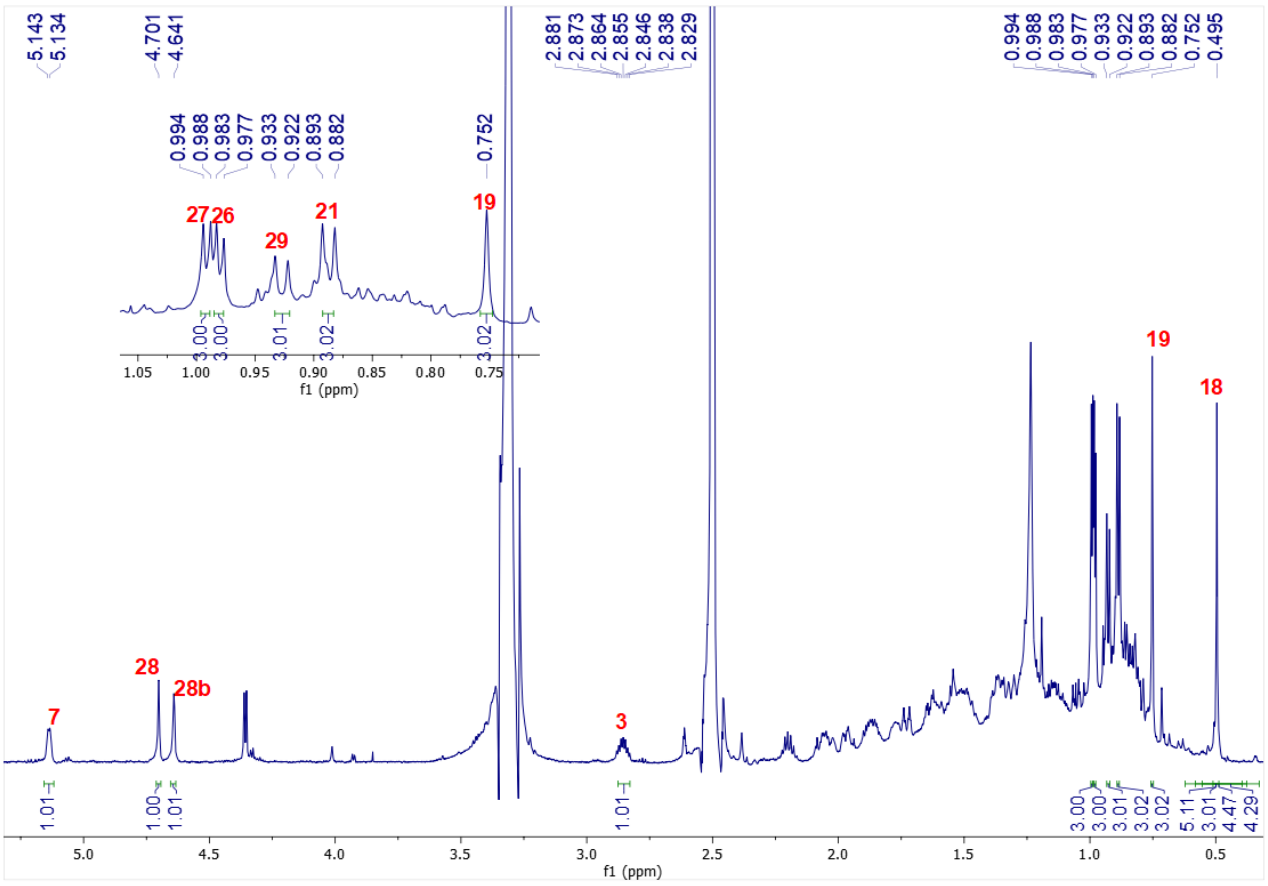

Figure 15S. The ^{1}H NMR spectrum of **4** in $CDCl_3$

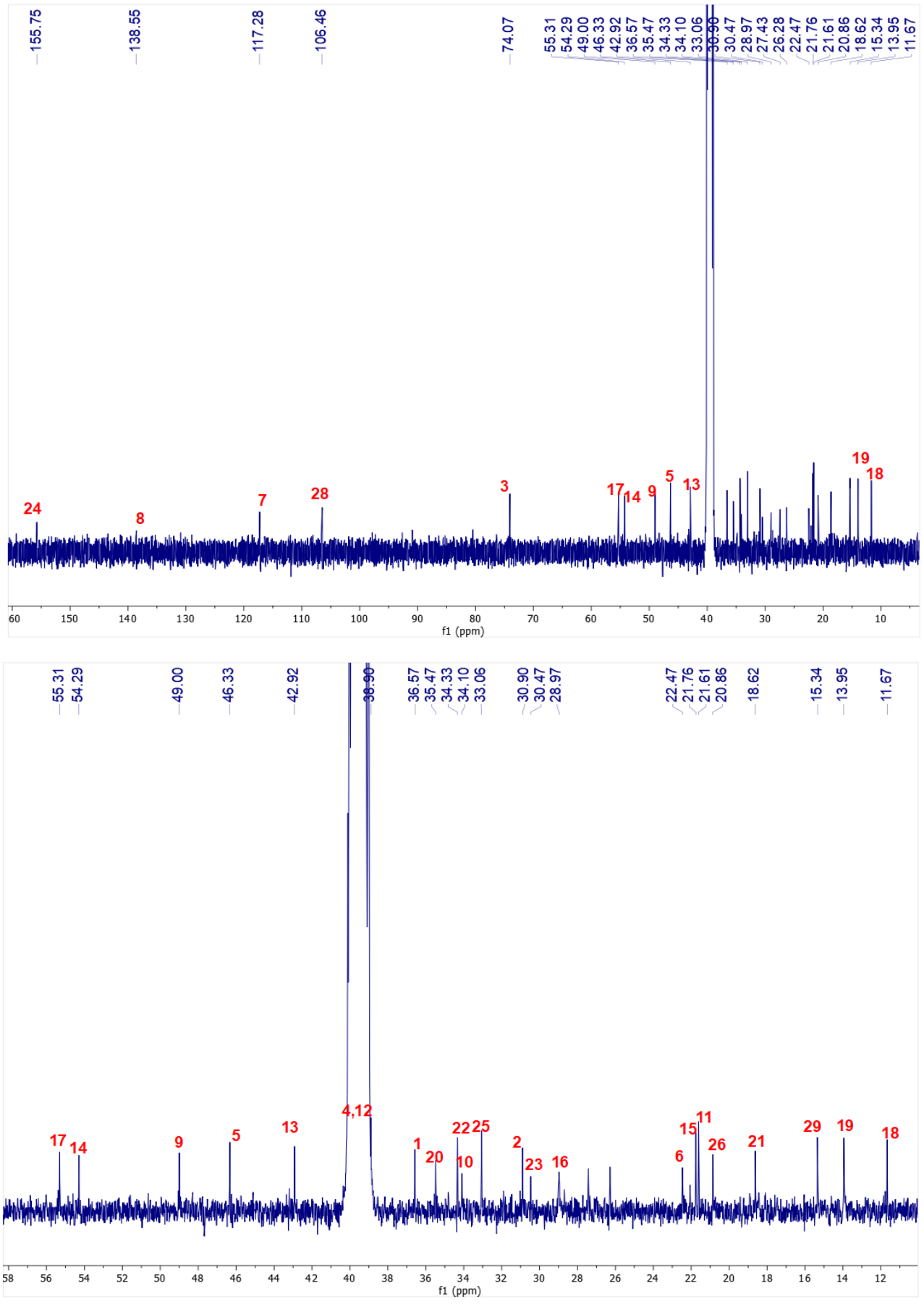

Figure 16S. The ^{13}C NMR spectrum of **4** in $CDCl_3$

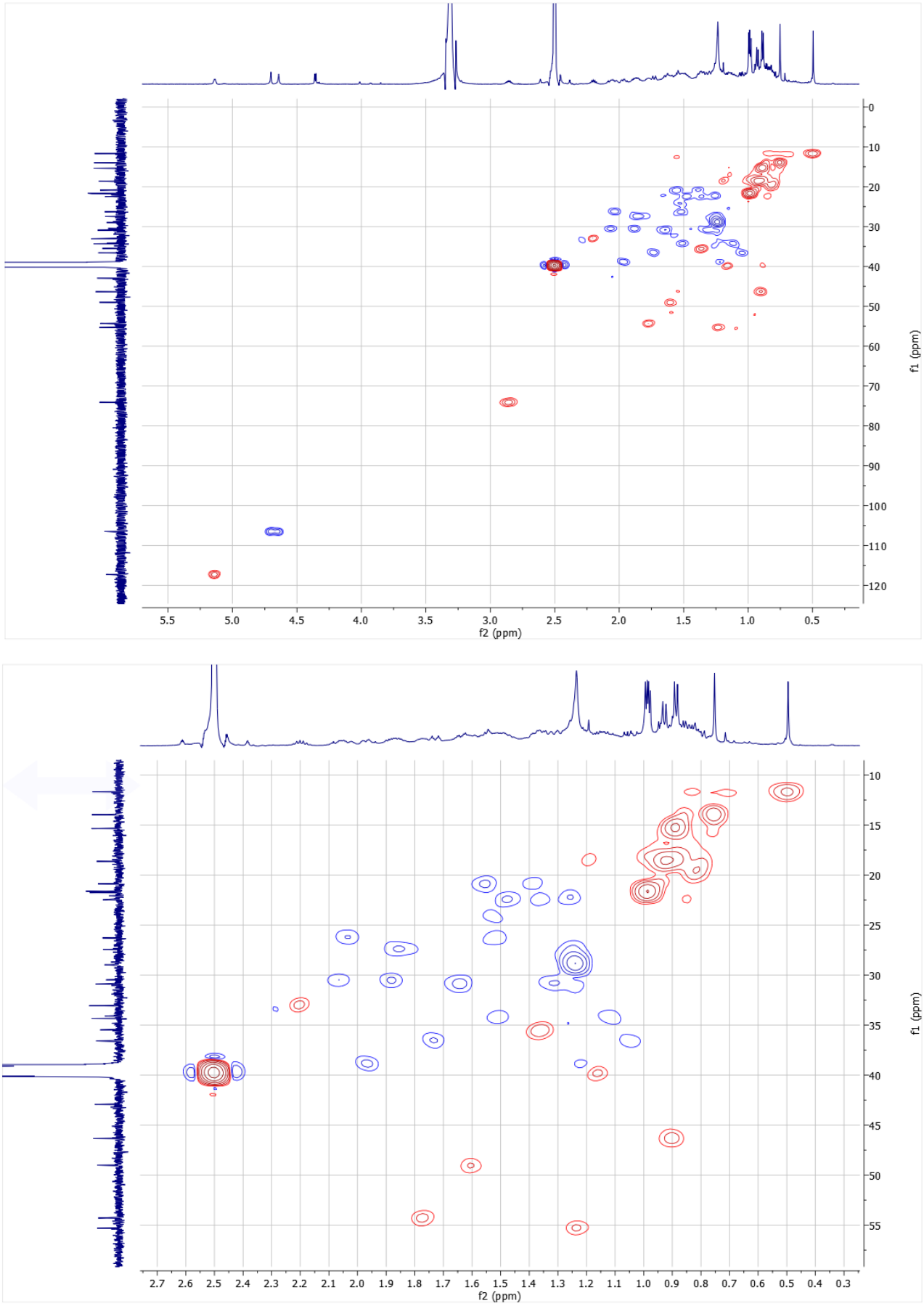

Figure 17S. The HSQC spectrum of **4** in $CDCl_3$

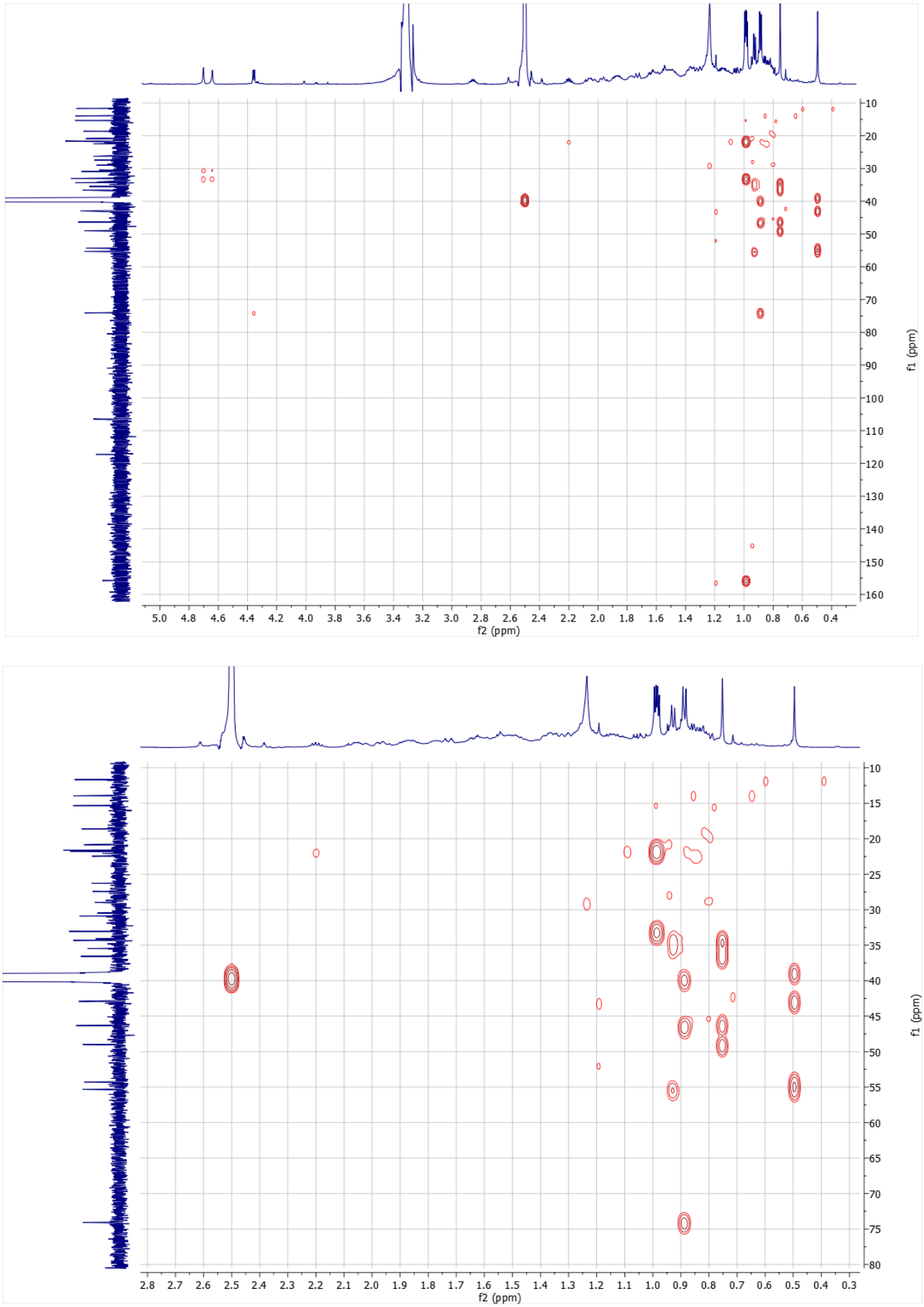

Figure 18S. The HMBC spectrum of **4** in $CDCl_3$

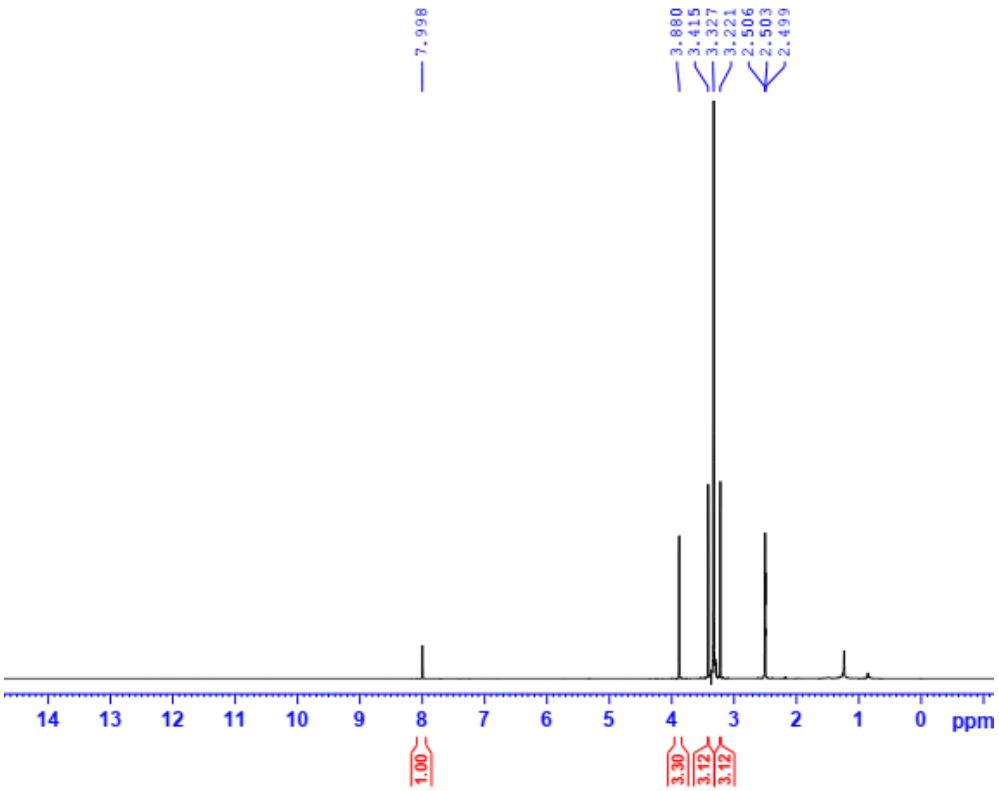

Figure 19S. The ^{1}H NMR spectrum of **5** in DMSO-d_6

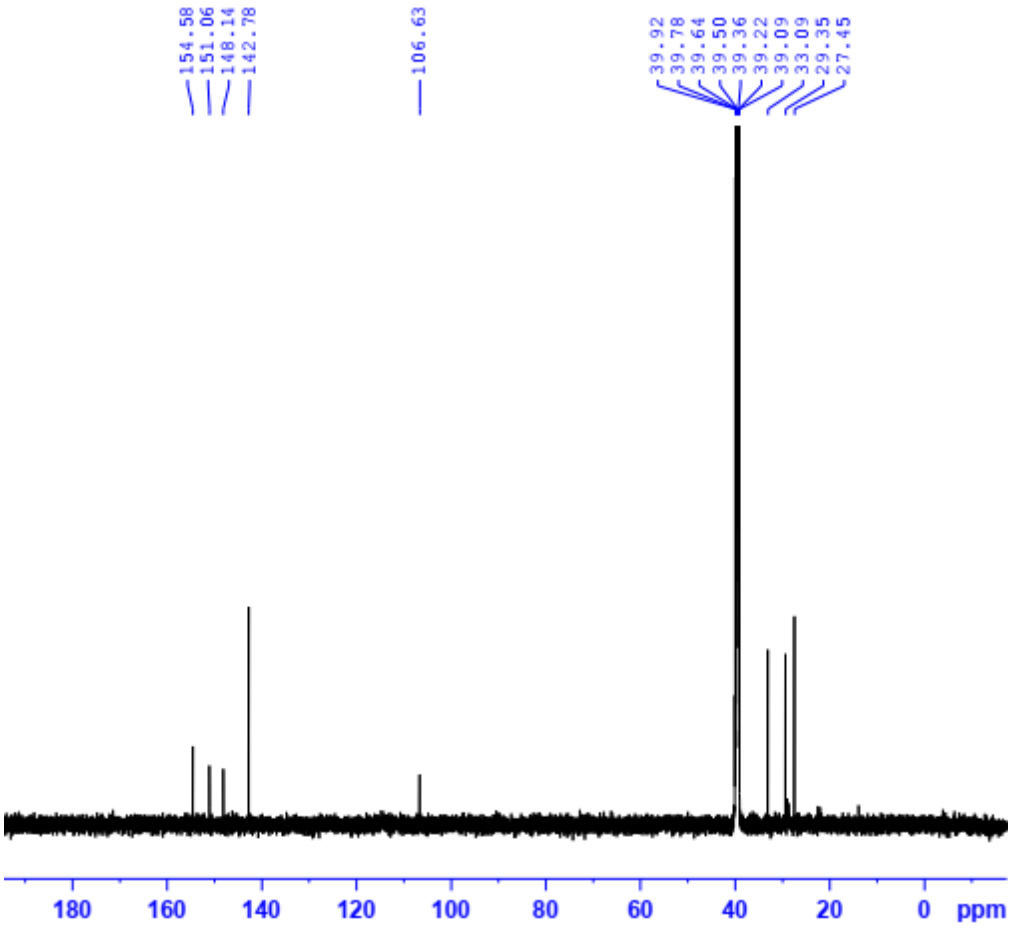

Figure 20S. The ^{13}C NMR spectrum of **5** in DMSO-d_6

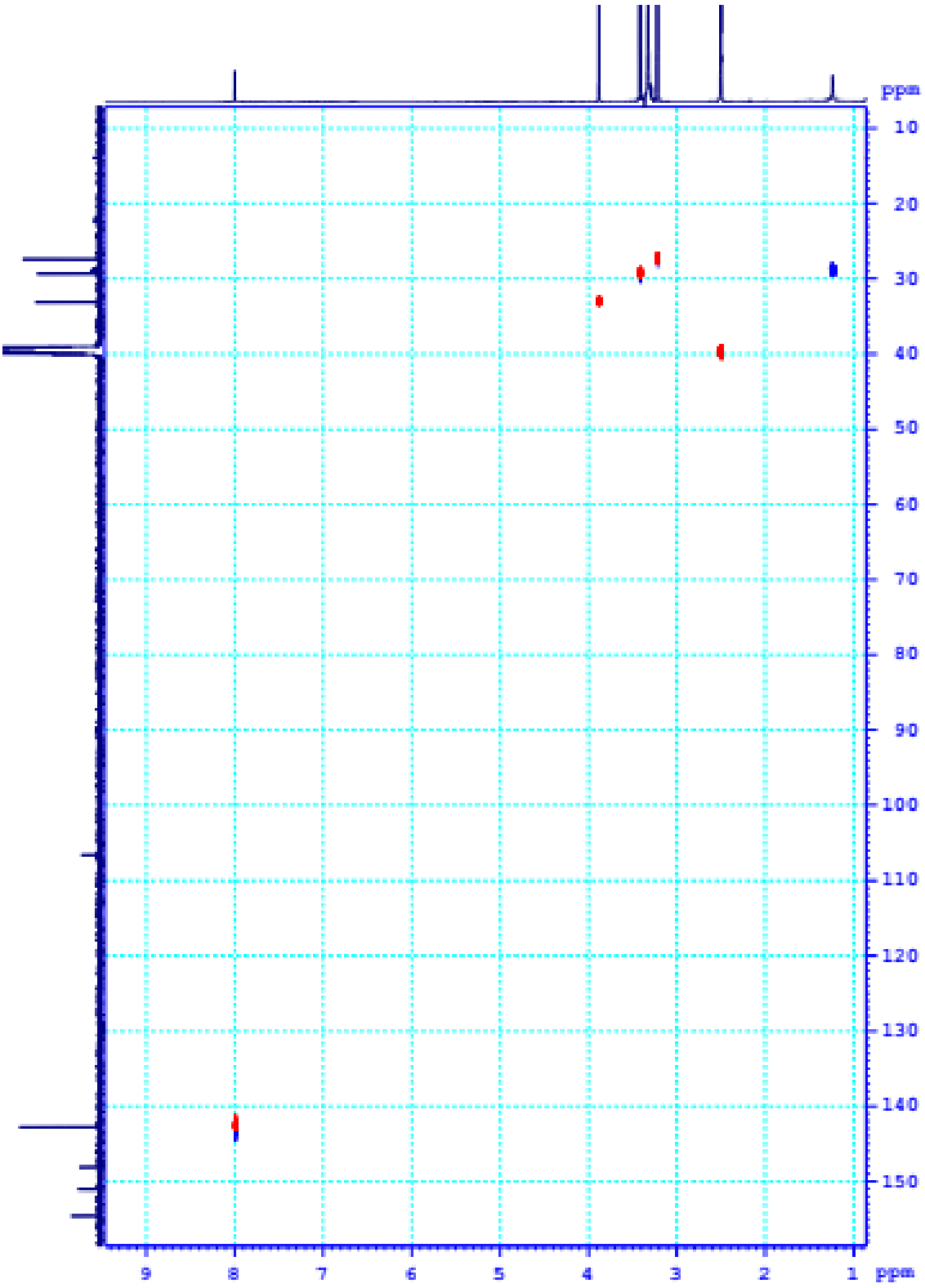

Figure 21S. The HSQC spectrum of **5** in DMSO-d_6

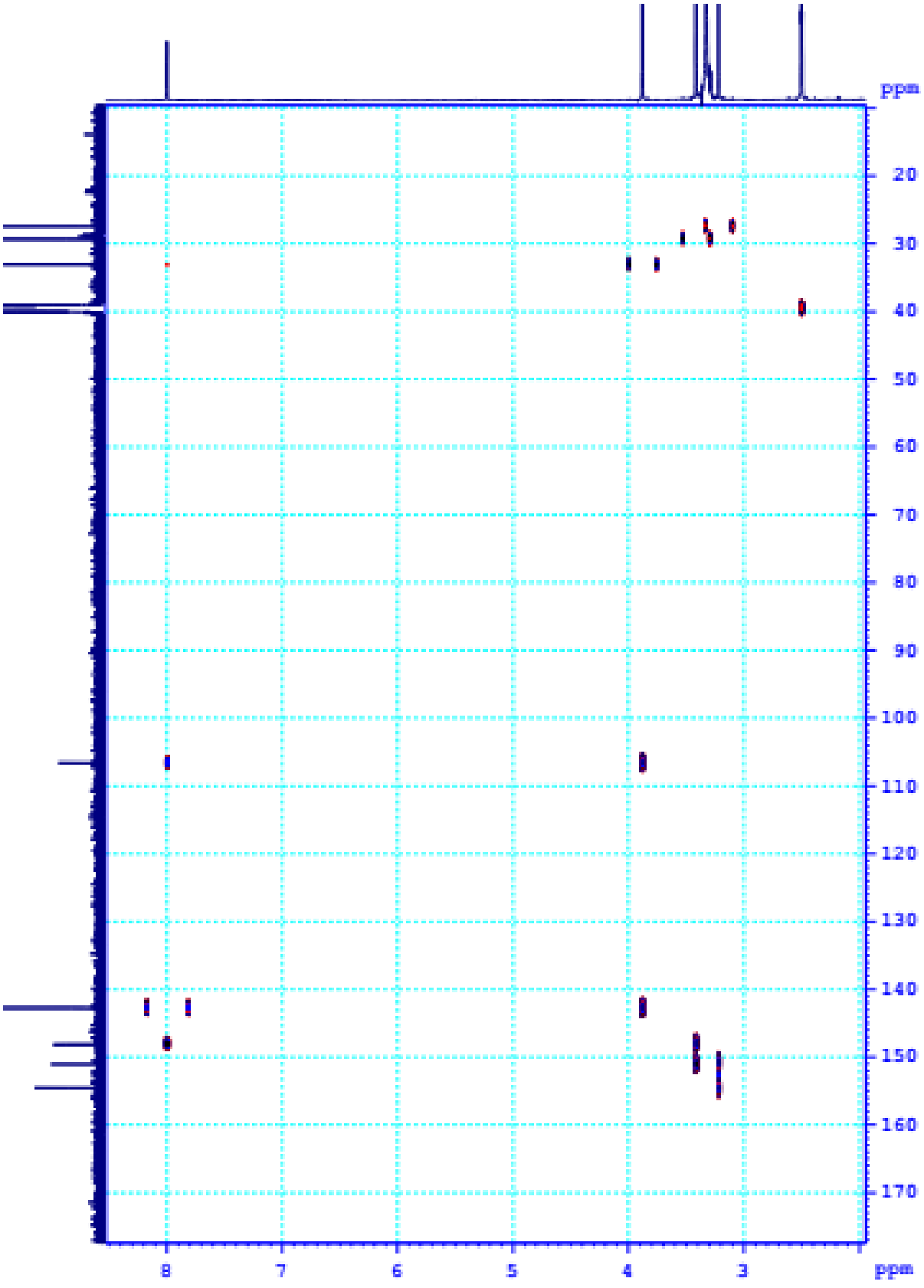

Figure 22S. The HMBC spectrum of **5** in DMSO-d_6

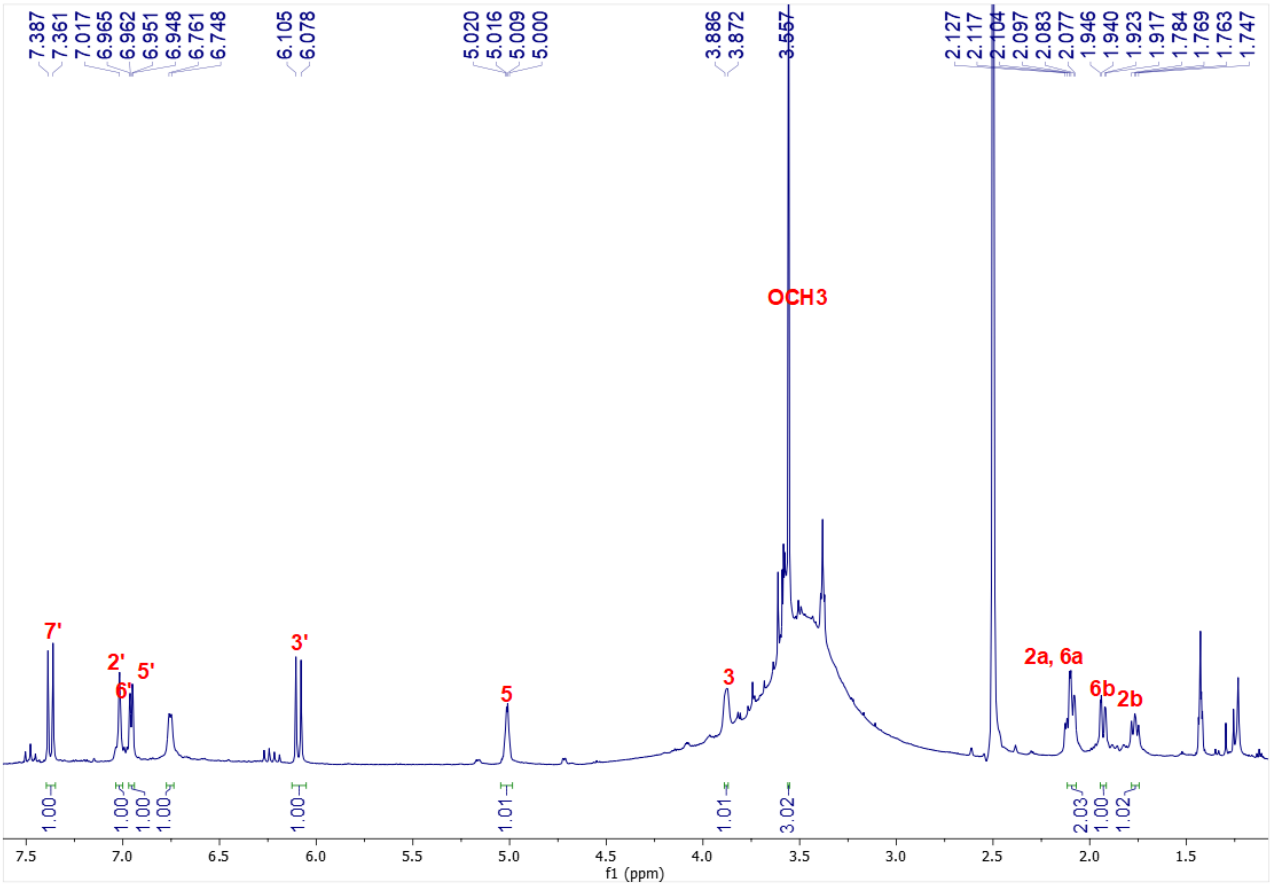

Figure 23S. The ^{1}H NMR spectrum of **6** in DMSO-d_6

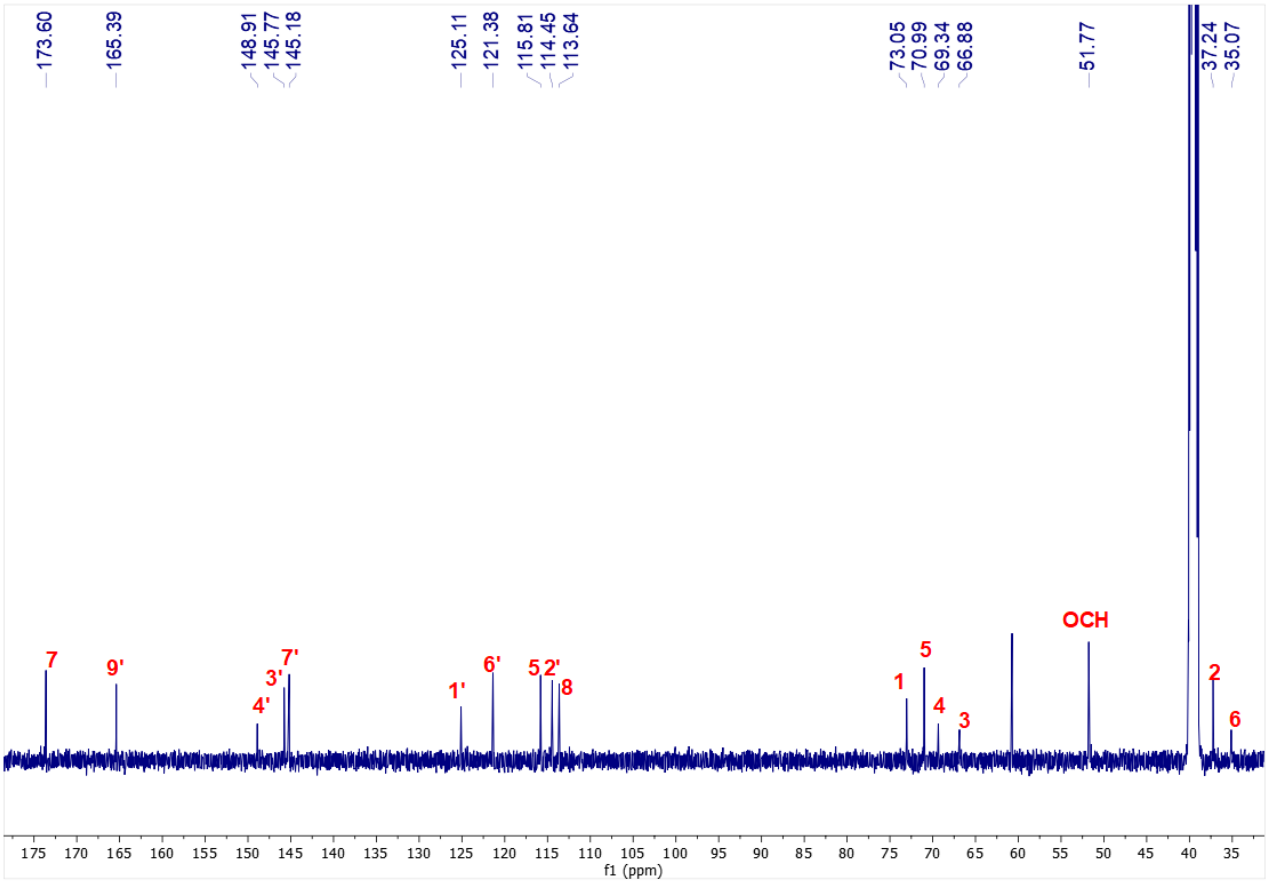

Figure 24S. The ^{13}C NMR spectrum of **6** in DMSO-d_6

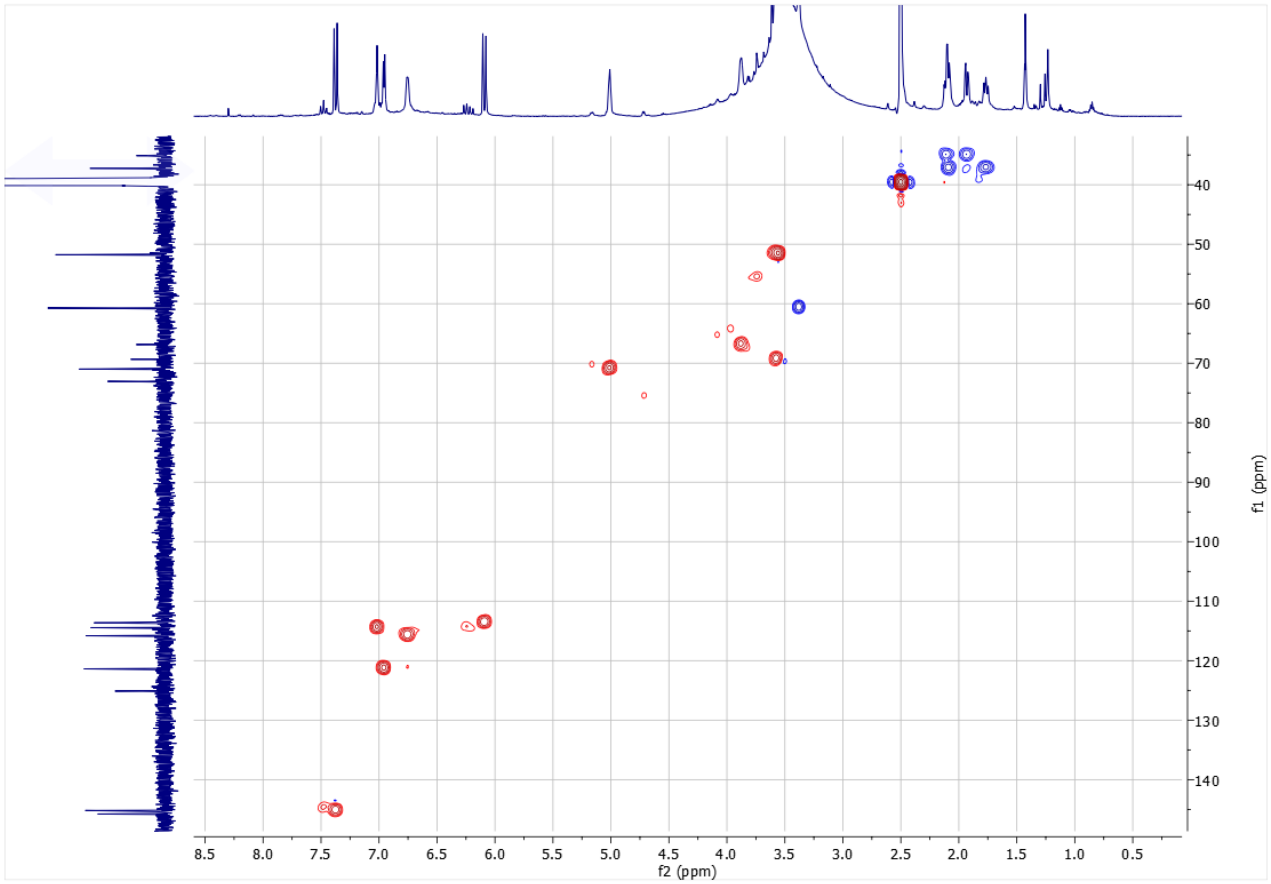

Figure 25S. The HSQC spectrum of of **6** in DMSO-d_6

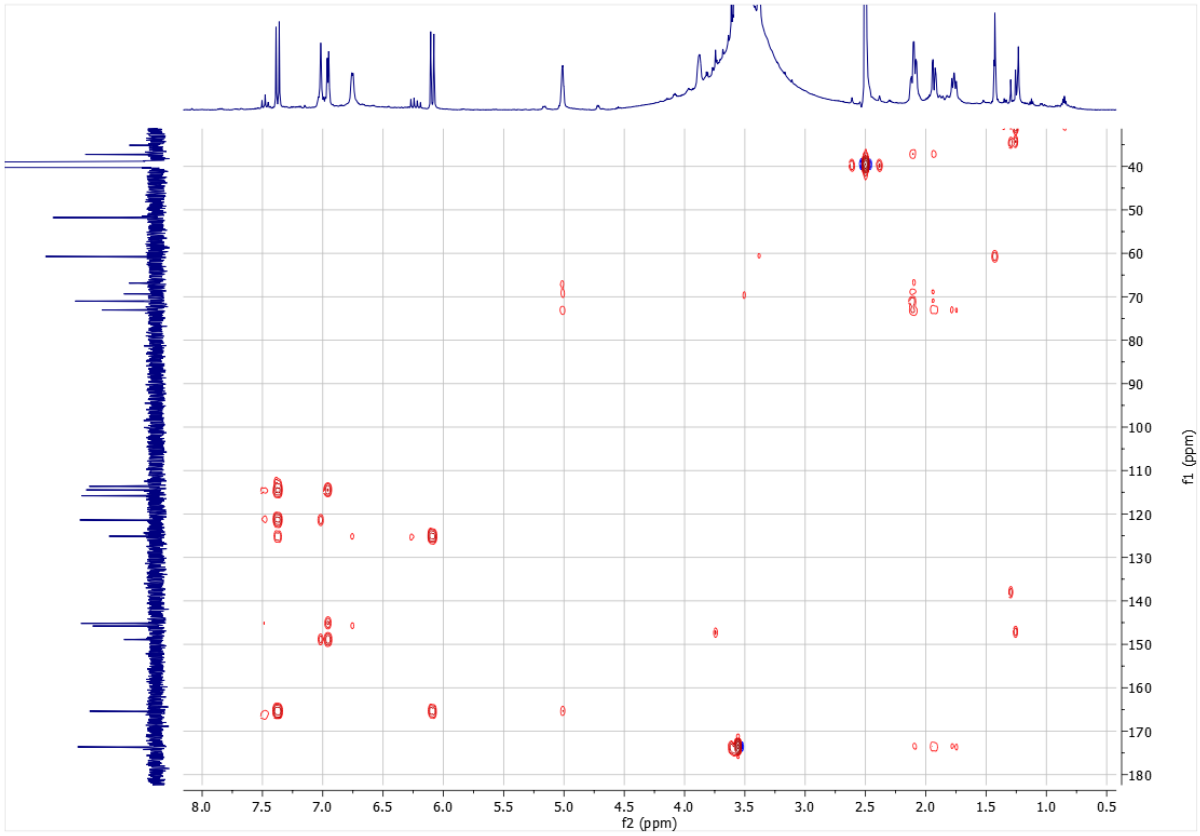

Figure 26S. The HMBC spectrum of **6** in DMSO-d_6

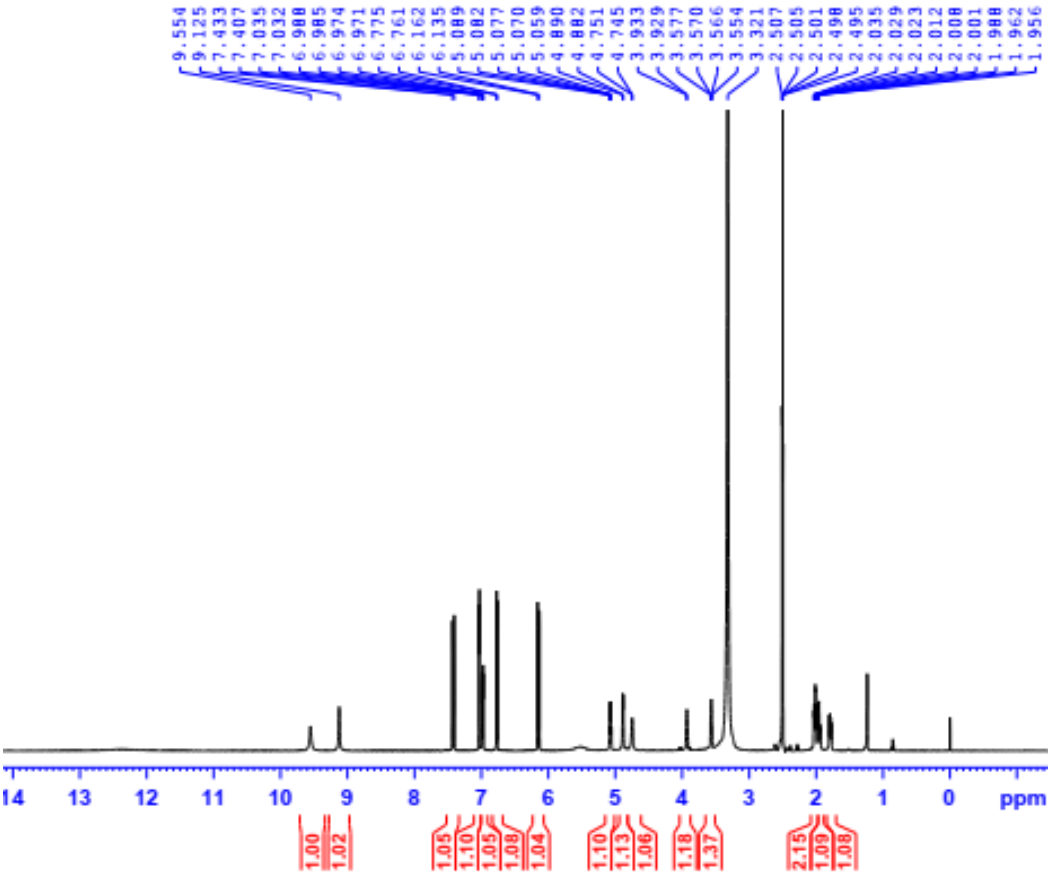

Figure 27S. The ^{1}H NMR spectrum of **7** in DMSO-d_6

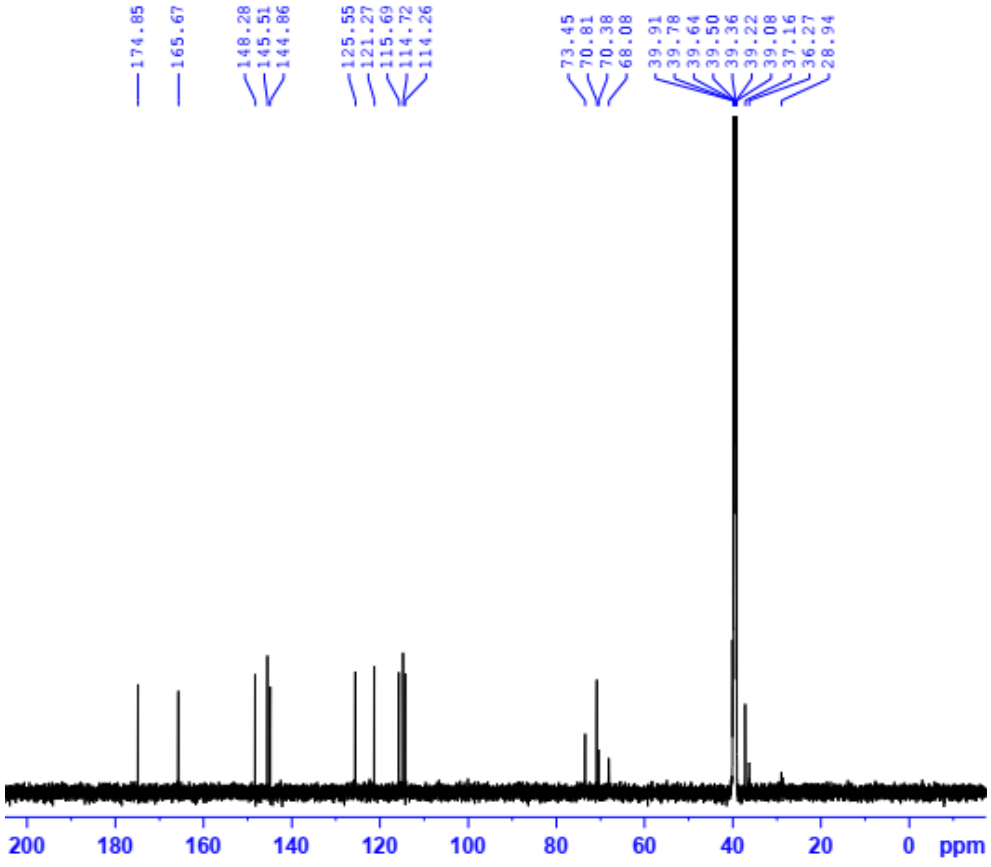

Figure 28S. The ^{13}C NMR spectrum of **7** in DMSO-d_6

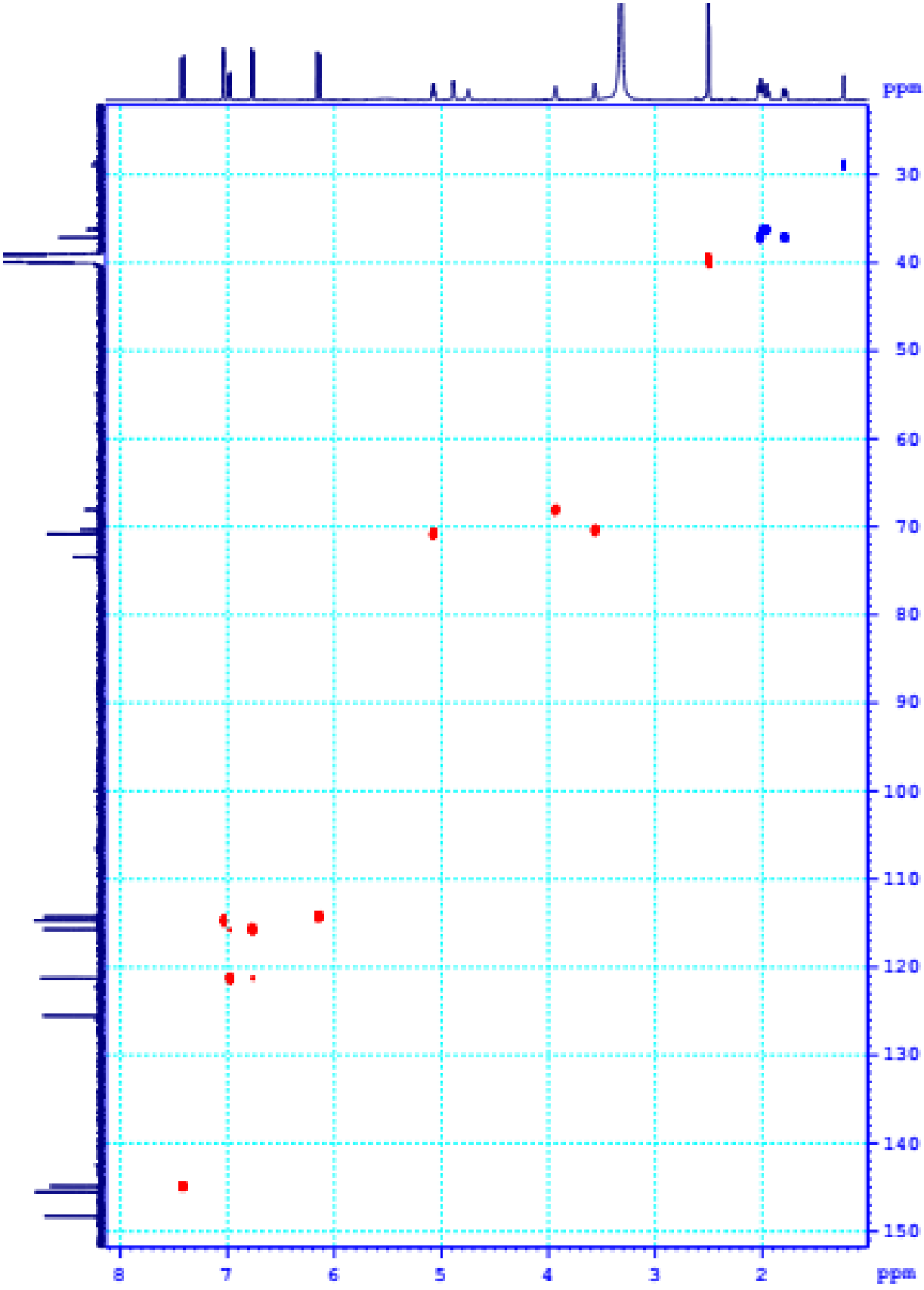

Figure 29S. The HSQC spectrum of **7** in DMSO-d_6

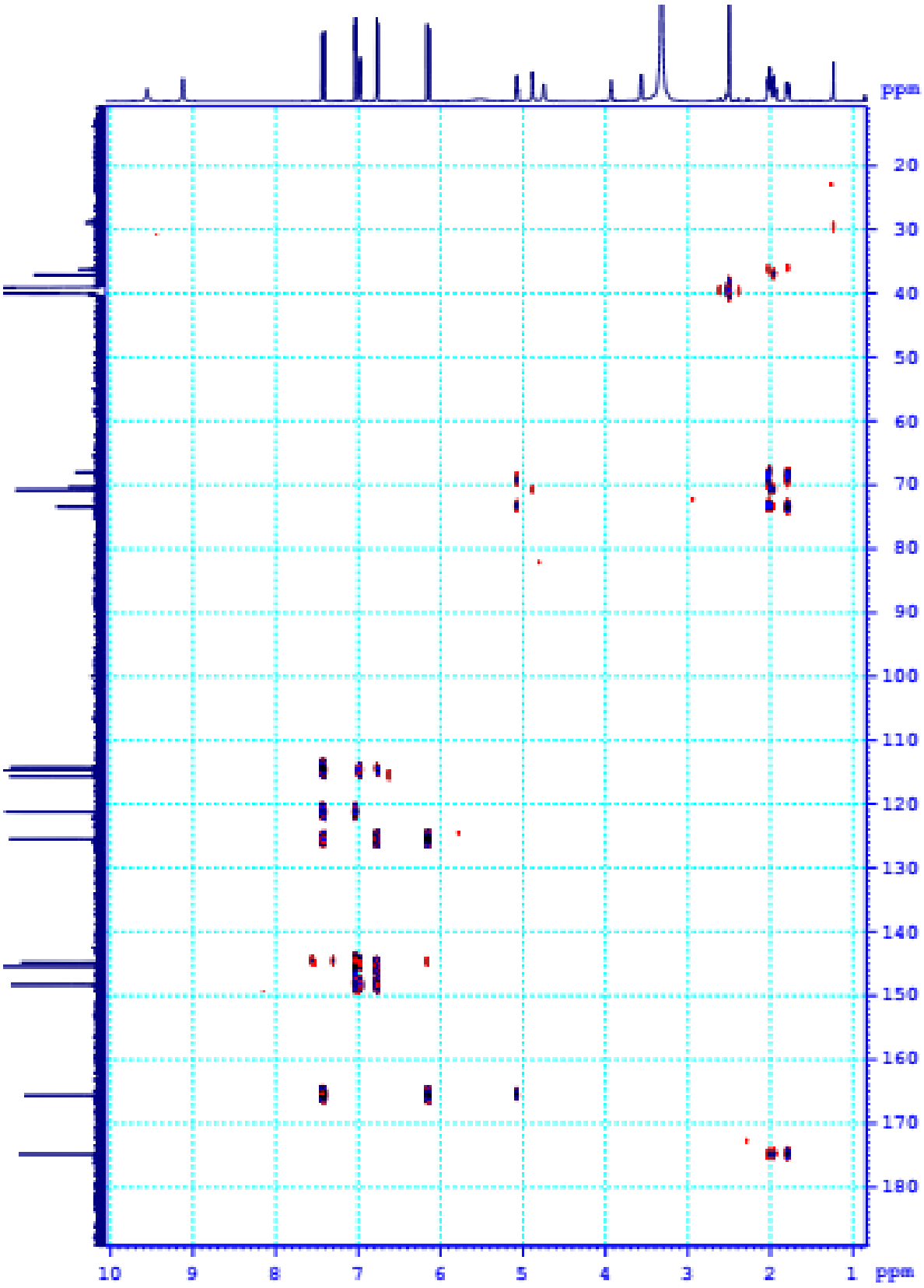

Figure 30S. The HMBC spectrum of **7** in DMSO-d_6

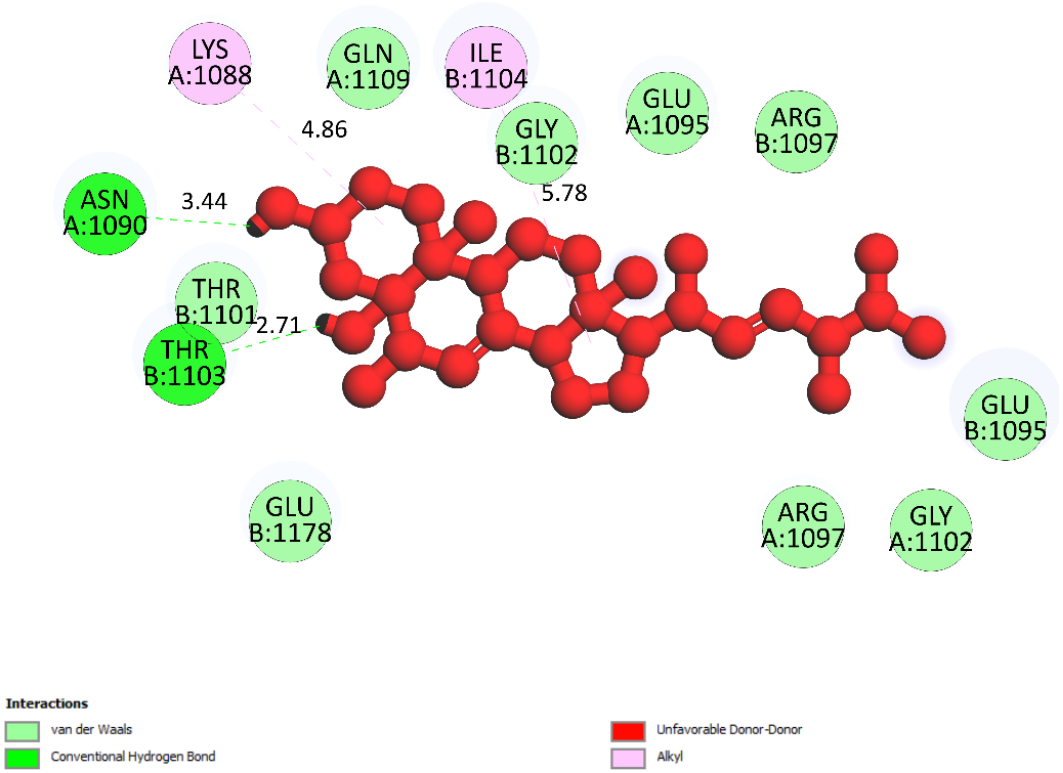

Figure 31S. The important ligand interactions between pose 119, compound **3** and 3TOP enzyme

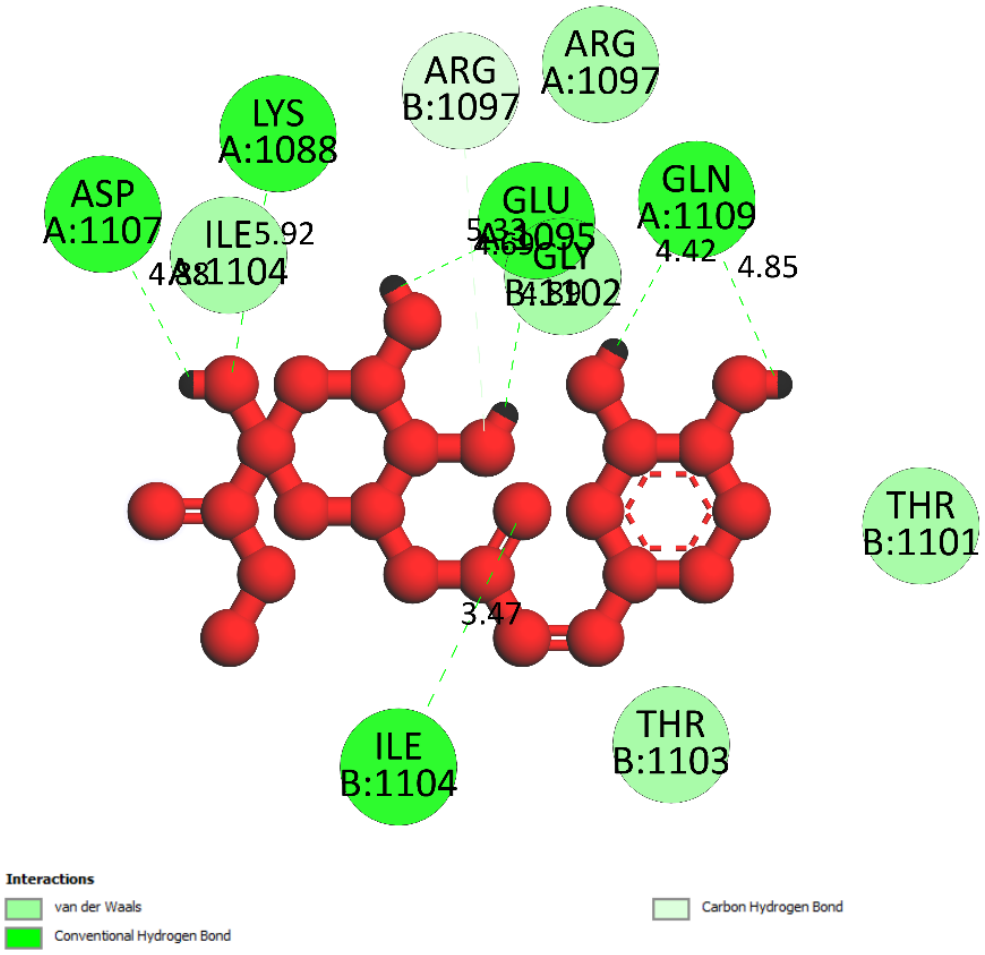

Figure 32S. The significant interaction between the best pose 394/ compound 6 and 3TOP on 2D diagram, not enough interacions

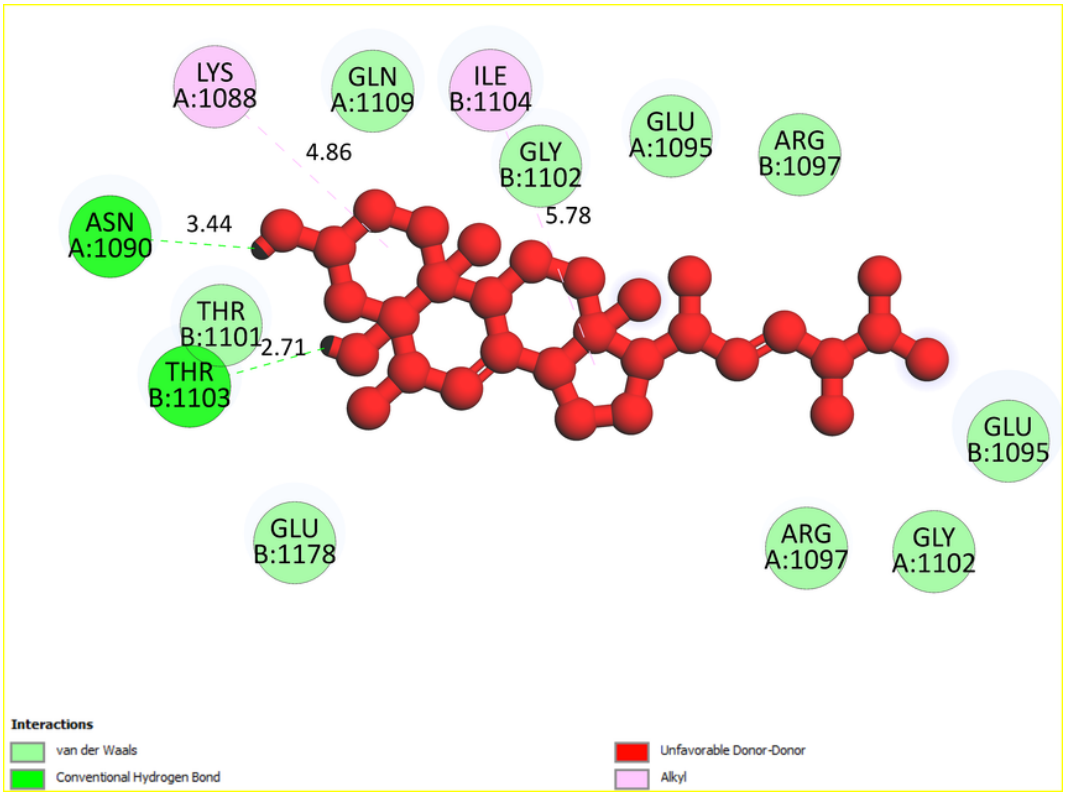

Figure 33S. The significant interactions between pose 491/compound **1** and 3TOP on 2D diagram, not good interactions

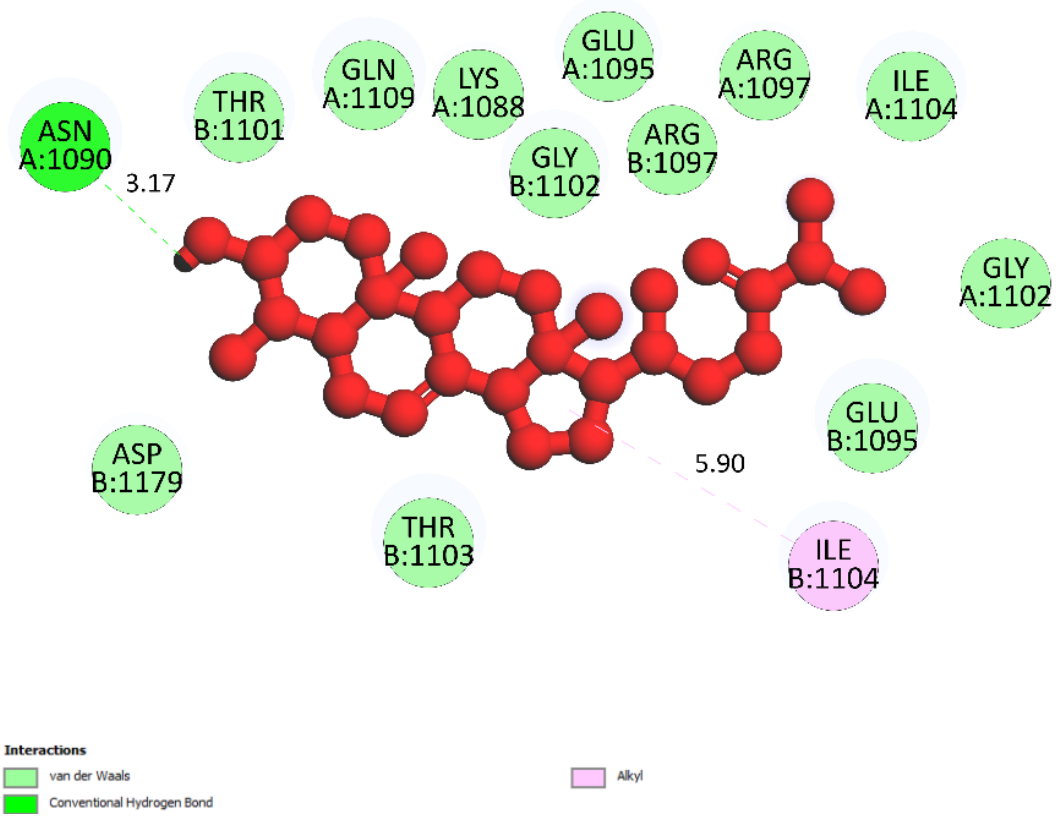

Figure 34S. The significant ligand interaction model between pose 237, compound **4** and 3TOP enzyme, not good interaction

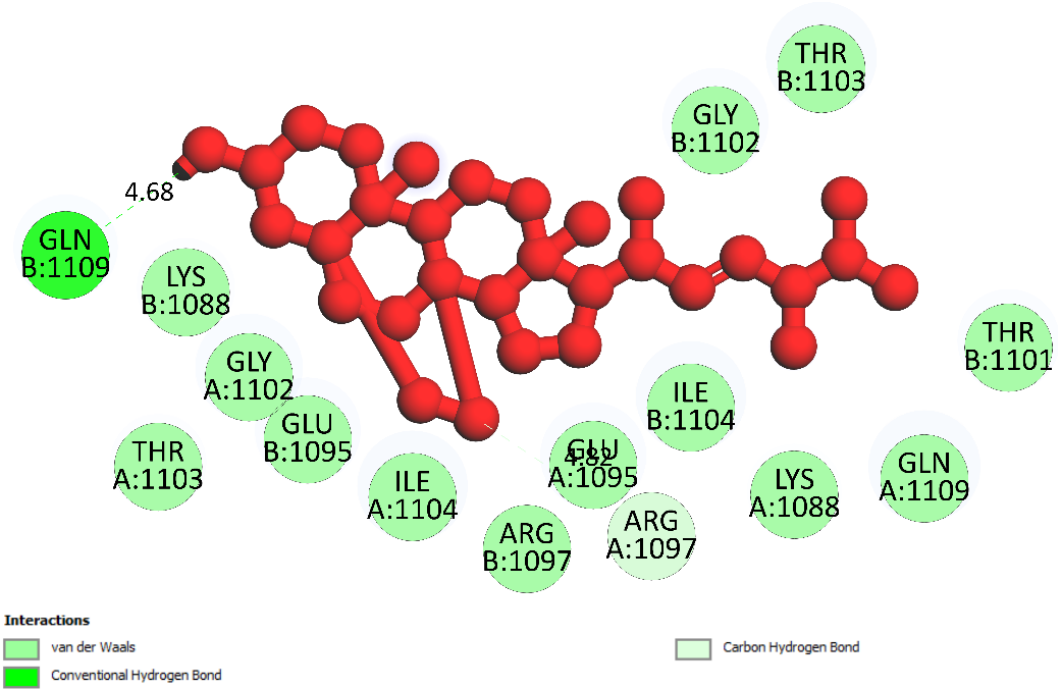

Figure 35S. The significant ligand interactions between **pose 155**, compound **2** and 3TOP

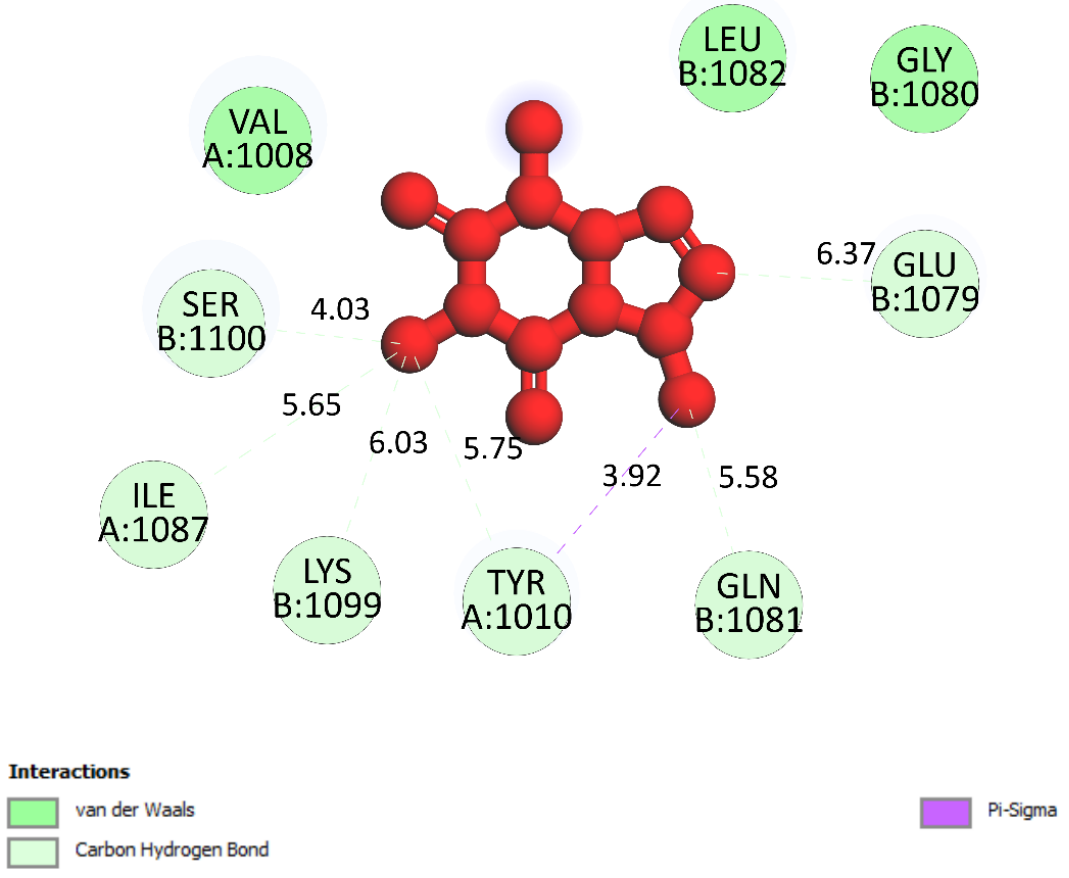

Figure 36S. The significant interactions between **pose 355**, compound **5** and 3TOP enzyme, not good interactions

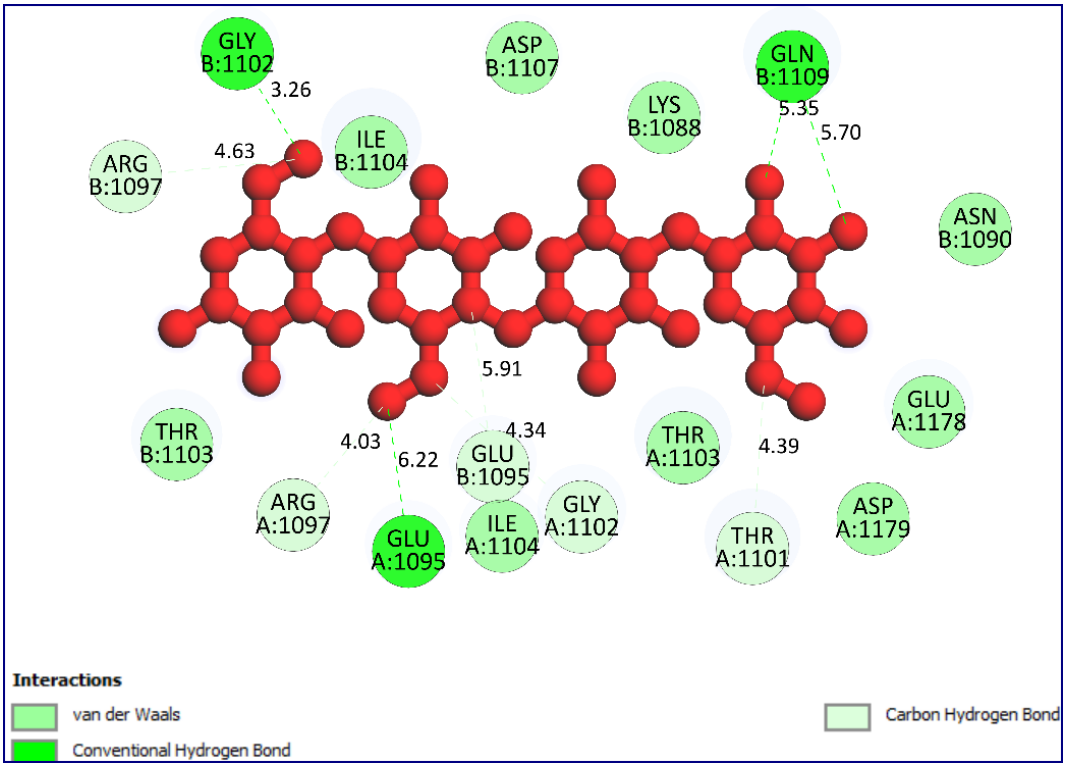

Figure 37S. The Acarbose, pose 61/ positive control drug docked to 3TOP enzyme.

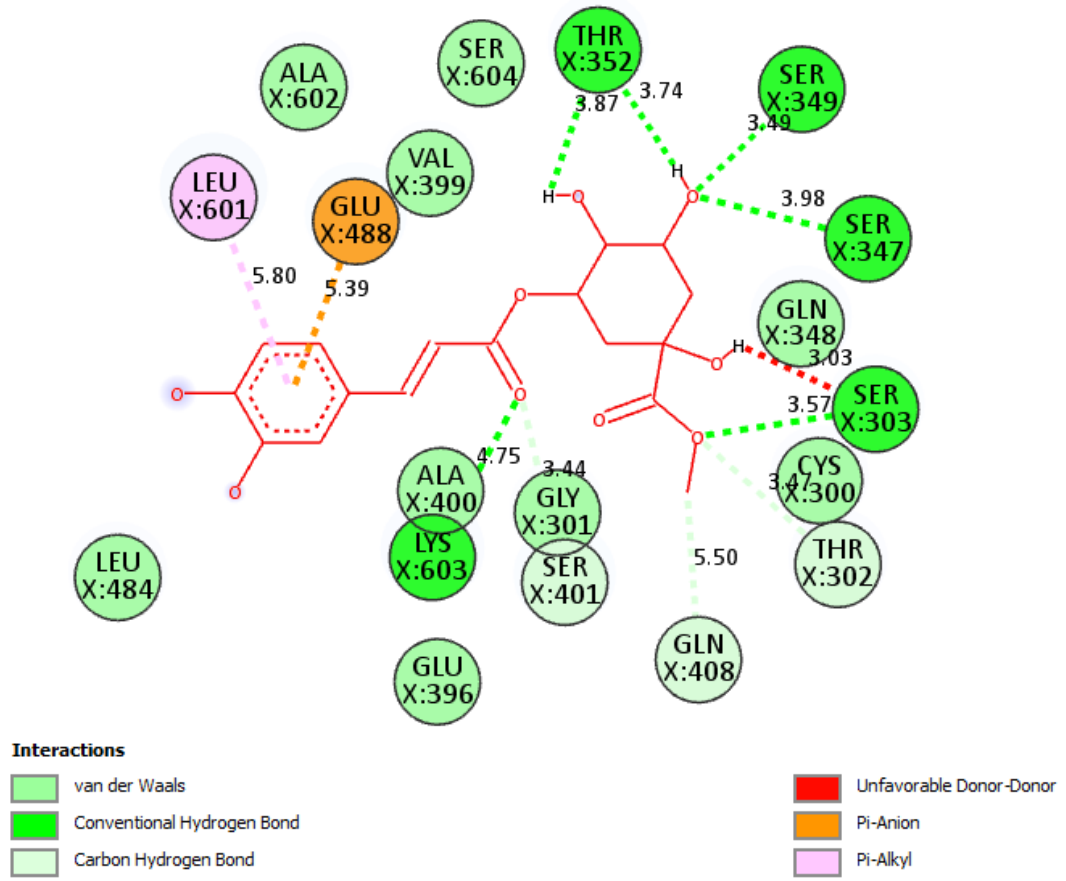

Figure 38S. The most important ligand interactions forming between pose 992/compound (**6**) and 2VF5 on one 2D diagram: good interaction.

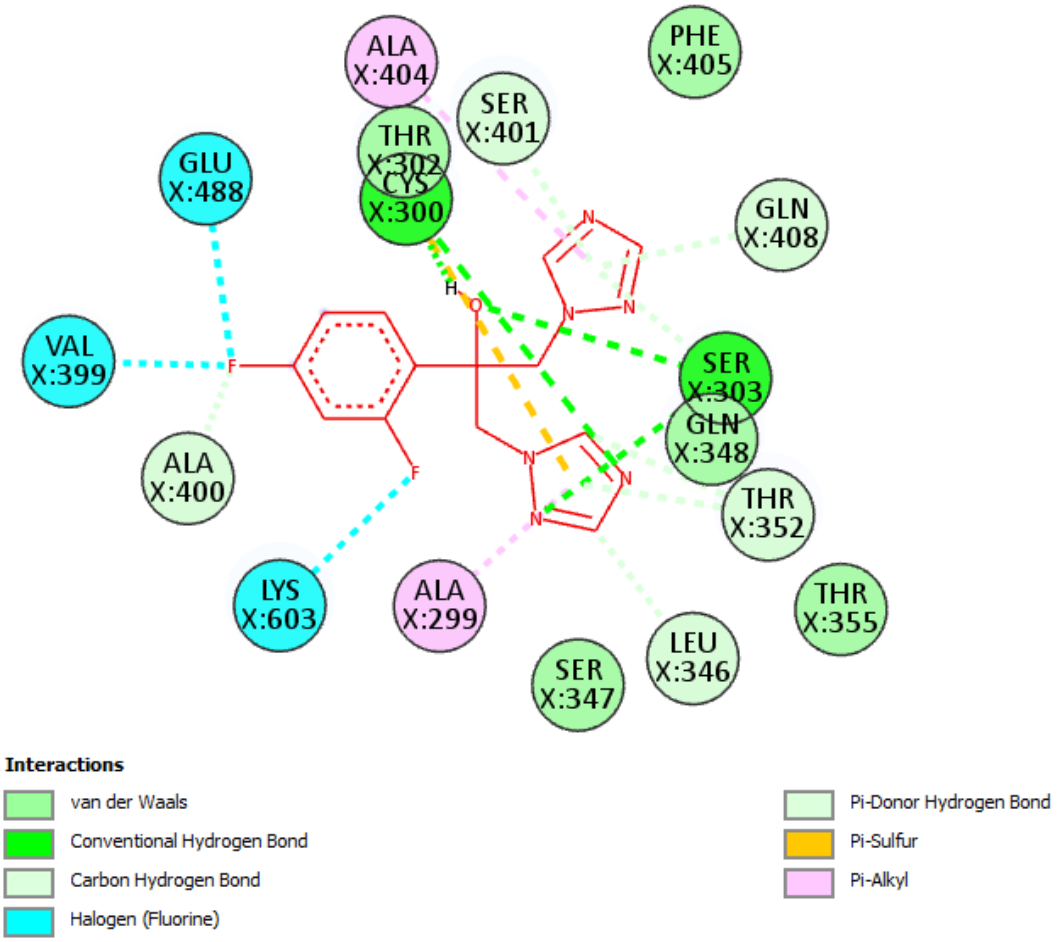

Figure 39S. The significant ligand interaction between pose 81 and 2VF5 enzyme on one 2D diagram.

Table 1S. Spectroscopic data of ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR of ergosterol peroxide (**2**) and cerevisterol (**3**).

No	ergosterol peroxide (**2**)[a]		cerevisterol (**3**)[a]	
	δ_C	δ_H	δ_C	δ_H
1	34.7	1.93(1H, m), 1.68 (1H, dd, 13.8, 3.6)	33.0	
2	30.1	1.50 (1H, m), 1.94 (1H, m)	31.9	
3	66.4	3.99 (1H, m)	67.7	4.08 (1H, m)
4	37.0	1.88 (1H, m), 2.10 (1H, m)	39.5	
5	82.1		76.0	
6	135.4	6.24 (1H, d, 8.4)	73.7	3.62 (brs)
7	130.7	6.50 (1H, d, 8.4)	117.5	5.35 (1H, t, 2.4)
8	79.4		144.0	
9	51.1		43.5	
10	36.9		37.1	
11	20.6		22.0	
12	39.4		39.2	
13	44.5		43.8	
14	51.7		54.7	
15	23.4		22.7	
16	28.6		29.2	
17	56.2	1.25 (1H, m)	56.0	
18	18.1	0.88 (3H, s)	12.3	0.60 (3H, *s*)
19	12.8	0.81 (3H, s)	18.4	1.08 (3H, *s*)
20	39.7	1.96 (1H, m)	40.3	
21	20.8	0.99 (3H, d, 6.6)	21.1	1.03 (3H, d, 6.6)
22	135.2	5.16 (1H, d, 15.0, 8.4)	135.3	5.23 (1H, dd, 15.6, 7.2)
23	132.3	5.21 (1H, m, H-22)	132.2	5.17 (1H, dd, 15.0, 7.4)
24	42.7	1.83 (1H, m)	42.5	
25	33.0	1.48 (1H, m)	33.1	
26	19.8	0.82 (3H, d, 6.6)	19.9	0.84 (3H, d,7.2)
27	19.9	0.83 (3H, d, 6.6)	19.6	0.83 (3H, d, 6.6)
28	17.5	0.91 (3H, d, 6.6)	17.6	0.92 (3H, d, 7.2)

δ in ppm; J in Hz; [a]$CDCl_3$

Table 2S. Spectroscopic data of ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR of gramisterol (**4**) and caffeine (**5**).

No	gramisterol (**4**)[a]		caffeine (**5**)[b]	
	δ_C	δ_H	δ_C	δ_H
1	36.5		27.9	3.40 (s, 1-CH_3)
2	30.9		151.7	
3	74.0	2.85 (1H, m)	29.7	3.58 (s, 3-CH_3)
4	39.8		148.7	
5	46.3		107.6	
6	22.4		155.4	
7	117.2	5.14 (1H, d, 4.2)	33.5	3.99 (s, 7-CH_3)
8	138.5		141.4	7.52 (1H, s)
9	49.0			
10	34.1			
11	21.6			
12	39.0			
13	42.9			
14	54.2			
15	21.7			
16	28.9			
17	55.3			
18	11.6	0.54 (3H, s)		
19	13.9	0.75 (3H, s)		
20	35.4			
21	18.6	0.89 (3H, d, 6.6)		
22	34.3			
23	30.4			
24	155.7			
25	33.0			
26	20.8	0.97 (3H, d, 6.6)		
27	21.7	0.98 (3H, d, 6.6)		
28	106.4	4.70 (1H, s); 4.64 (1H, s)		
29	15.3	0.93 (3H, d, 6.6)		

δ in ppm; J in Hz; [a] $CDCl_3$, [b] DMSO-d_6

Table 3S. Spectroscopic data of ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR of methyl 5-*O*-caffeoylquinate (**6**) and chlorogenic acid (**7**).

No	methyl 5-*O*-caffeoylquinate (**6**)[a]		chlorogenic acid (**7**)[a]	
	δ_C	δ_H	δ_C	δ_H
1	73.0	-	73.5	-
2	37.2	2.13 (1H; m; H2a) 1.79 (1H; m; H2b)	37.2	2.04 (1H; m; H2a) 1.81 (1H; dd; 13.2; 7.8; H2b)
3	66.9	3.88 (1H; m)	68.1	3.93 (1H; d; 2.4)
4	69.3	3.62 (1H; m)	70.4	3.55-3.58 (1H; m)
5	71.0	5.02 (1H; m)	70.8	5.06-5.09 (1H; m)
6	35.1	2.13 (1H; m; H6a) 1.92 (1H; dd; 13.2; 3.0; H6b)	36.3	2.04 (1H; m; H6a) 1.96 (1H; dd; 13.2; 3.6; H6b)
7	173.6	-	174.9	-
1’	125.1	-	125.6	-
2’	114.4	7.02 (1H; s)	114.7	7.04 (1H; d; 1.8)
3’	145.8	-	144.9	-
4’	148.9	-	148.3	-
5’	115.8	6.76 (1H; d; 6.6)	115.7	6.78 (1H; d; 8.4)
6’	121.4	6.97 (1H; d; 7.2)	121.3	6.99 (1H; dd; 8.4; 1.8)
7’	145.2	7.39 (1H; d; 15.6)	145.5	7.43 (1H; d; 15.6)
8’	113.6	6.11 (1H; d; 15.6)	114.3	6.16 (1H; d; 16.2)
9’	165.4	-	165.7	-
OCH_3	51.8	3.56 (3H, s)		

δ in ppm; J in Hz.; [a] DMSO-d_6

Table 4S. The significant docking results of compound (**1-7**), and Acarbose (postive control) have been docked to **3TOP**: enzyme to explain and analyze the significant interaction results in the ligand interaction model

Entry	Pose[a]	Free Gibbs energy [b]	K_i[c]	The number of Hydrogen [d]	The character and bond length[e]
Comp 7	235	-4.98	224.1	8	A:Lys 1088:N – Pose 235:O (2.80 Å); A:Gln1109:N - Pose 235:O (3.06 Å); B:Thr 1103:O - Pose 235:O (2.71 Å); Pose 235:H - Glu1095:O (1.71 Å); Pose 235:H - B:Glu 1095:O (2.08 Å); Pose 235:H - B:Thr1103:O (2.05 Å); Pose 235:H - A:Gln 1109:O; (2.17 Å); Pose 235:H - A:Asn 1090:O (2.17 Å)
Comp 3	119	-8.84	0.330	4	B:Thr 1101:O – Pose 119:O (3.12 Å); B:Gly 1102:N – Pose 119:O (3.07 Å); B:Thr 1103:N – Pose 119:O (3.13 Å); Pose 119:H - A:Asn 1090:O (2.34 Å)
Acarbose	61	-8.81	0.35	0	
Comp 6	394	-5.38	114.0	11	A:Lys 1088:N – Pose 394:O (3.12Å); A:Lys 1088:N - Pose 394:O (2.85 Å); B:Ile 1104:N – Pose 394:O (2.88 Å); Pose 394:H - A:Gln 1109:O (2.25 Å); Pose 394:H - A:Glu 1095:O (1.80 Å); Pose 394:H - A:Glu 1095:O (2.05 Å); Pose 394:H - A:Gln 1109:O (1.74 Å); Pose 395:H - A:Gln 1109:O (3.25 Å); Pose 394:H - A:Glu 1095:O (1.80 Å); Pose 394:H - A:Glu 1095:O (2.05); Pose 394:H - A:Asp 1107:O (2.03Å)
Comp 1	491	-8.43	0.657	0	No hydrogen bonding
Comp 4	237	-9.49	0.11	01	Pose 237:H - A:Asn 1090:O (2.22 Å)
Comp 2	155	-8.71	0.412	01	Pose 155: H - B:Gln 1109:O (1.96 Å)
Comp 5	355	-4.59	429.8		No hydrogen bonding

Table 5S. The significant docking results of compound (**1-7**) to 2VF5 enzyme: PDB have been presented the significant interaction results and analyzed the ligand interaction model.

Entry	Pose [a]	Free Gibbs energy [b]	K_i[c]	The number of hydrogen [d]	The character and bond length[e]	Explaination: Good/bad interaction in ligand interaction model
Comp 7	49	-5.25	140	8	X:Ser 303:O – Pose 49:O (2.51 Å); X:Gln 348:N – Pose 49:O (2.63 Å); X:Ala 602:N – Pose 49:O (2.82 Å); Pose 49:H - X:Ser 303:O (2.11 Å); Pose 49: H - X:Leu 346:O (2.23 Å); Pose 49:H - X:Glu 488:O (1.79 Å); Pose 49:H - X:Glu 488:O (2.30 Å); Pose 49:H - X: Ala 602:O (2.10 Å).	Good interaction
Comp 6	992	-6.81	10.26	12	X:Ser303:N - :Pose 992:O (2.97Å); X:Ser 303:N - Pose 992:O (2.93 Å); X:Ser 303:OG - Pose 992:O (2.87 Å); X:Ser 303:OG - Pose 992:O (2.87 Å); X:Ser 347:O - Pose 992:O (2.80 Å); X:Ser 349:N - Pose 992:O (3.17 Å); X:Ser 349:O - Pose 992:O (2.58 Å); X:Thr 352:O - Pose 992:O (2.74 Å); X:Thr 352:O - Pose 992:O (2.92 Å); Pose 992:H - X:Thr 352:O (2.12 Å); Pose 992:H - X:Ser 349:O (2.39 Å); Pose 992:H - X:Thr 352:O (2.06 Å)	Good interaction
Fluconazole	81	-5.74	61.85	6	X:Cys 300:N – Pose 81:N (3.11 Å); X:Ser 303:N – Pose 81:O (2.97 Å); Ser 303:O – Pose 81:N (2.71 Å); X:Ser 303:O - :LIG1:O (2.75 Å); X:Ser 401:O – Pose 81:N (2.86 Å); Pose 81:H - X:Cys 300:O (2.26 Å)	Good interaction

Entry	Pose [a]	Free Gibbs energy [b]	K_i [c]	The number of hydrogen [d]	The character and bond length [e]	Explaination: Good/bad interaction in ligand interaction model
Comp 1	720	-9.96	0.05	1	Pose 720:H - X:Glu 488:O (1.98 Å)	Not full interactions: Functional group: 01 hydrogen bonding, Glu 488 to hydrogen atom of hydroxyl alcohol; Capping group (CA): no; Connecting unit (CU): 01 alkyl interaction from Ala 299 to carbon methyl.
Comp 2	329	-10.43	0.023	3	X:Thr 302:N – Pose 329:O (2.72 Å); X:Gln 348:N – Pose 329:O (2.67 Å); X:Ser 347:O – Pose 329:O (3.06 Å)	Bad interaction: 01 unfavorable donor-donor from Gln 348 to hydrogen atom of hydroxyl alcohol; (red color)
Comp 3	830	-10.17	0.035	3	X:Gly 301:N – Pose 930:O (2.88 Å); X:Asn 305:N – Pose 930:O (3.13 Å); X:Asn 305:N – Pose 930:O (1.99 Å)	Not full interactions: Functional group: 02 hydrogen bondings: Glu 488 to hydrogen atom of alcohol group; Ala 602 to hydrogen atom of alcohol group; Capping group (CA): 01 pi-alkyl from Leu 601 to cyclohexyl group on pose 830; Connecting unit (CU): no.
Comp 4	973	-10.44	0.022	0	-	Not full interactions: Functional group: no; Capping group (CA): 01 alkyl interaction from Leu 601 to cyclohexyl group; Connecting unit (CU): No

Entry	Pose [a]	Free Gibbs energy [b]	K_i [c]	The number of hydrogen [d]	The character and bond length [e]	Explaination: Good/bad interaction in ligand interaction model
Comp 5	177	-4.72	348	5	X:Ser 303:N – Pose 177:N (2.97 Å); X:Ser 303:OG - Pose 177:N (3.08 Å); X:Ser 349:O - :LIG1:O (2.60 Å) X:Thr 352:O – Pose 177:O (3.01 Å) X:Lys 603:N – Pose 177:O (3.20 Å)	Not full interactions: Functional group: 03 hydrogen bondings from Ser 349 and Thr 352 to oxygen atom of carbonyl group and Ser 303 to nitrogen atom on pose; Capping group (CA): no; Connecting unit (CU): 03 caarbon hydrogen bond interactions from Cys and Ser 303 to methyl group and Lys 603 to another methyl group on pose.